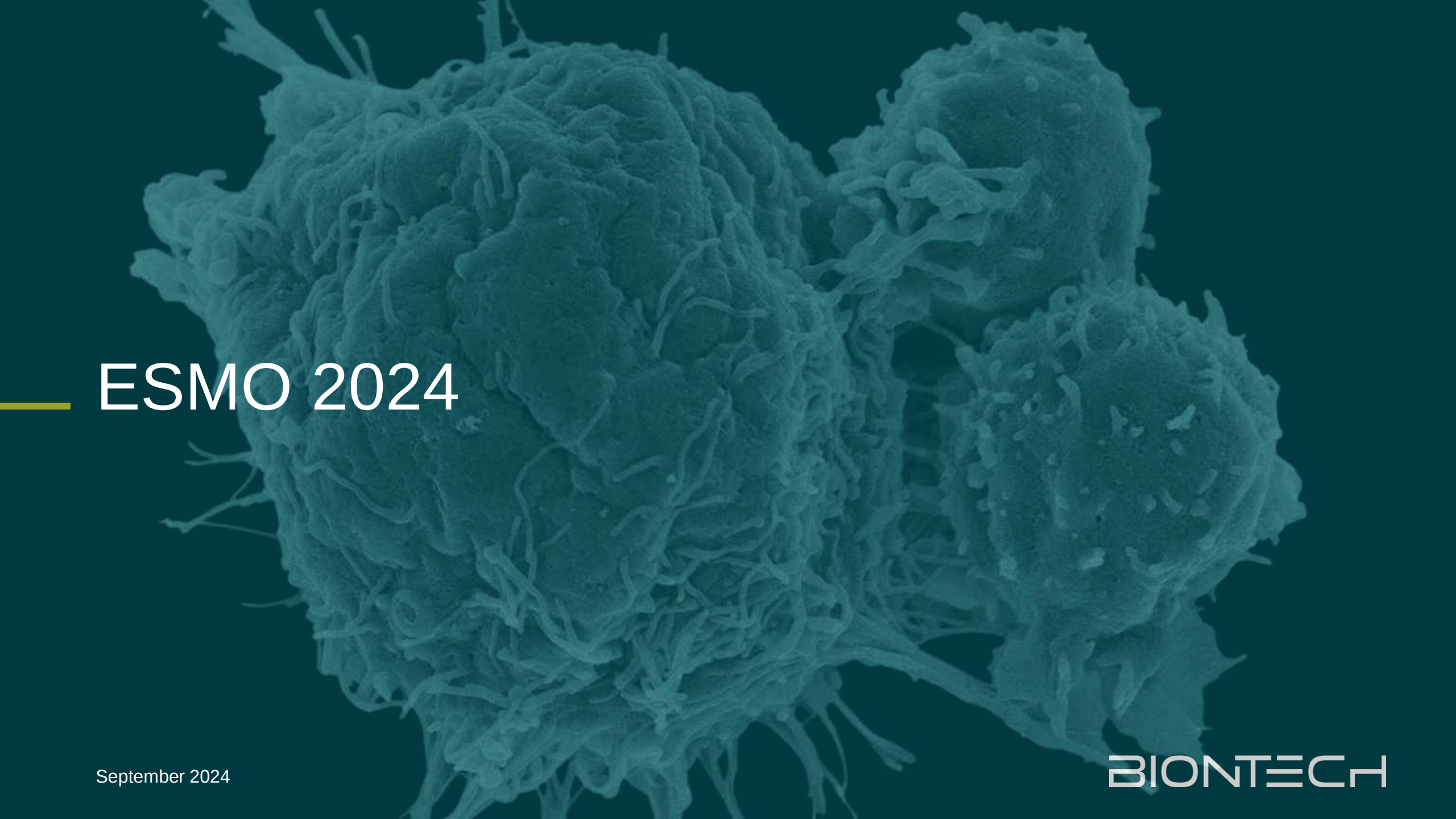




ESMO 2024

September 2024

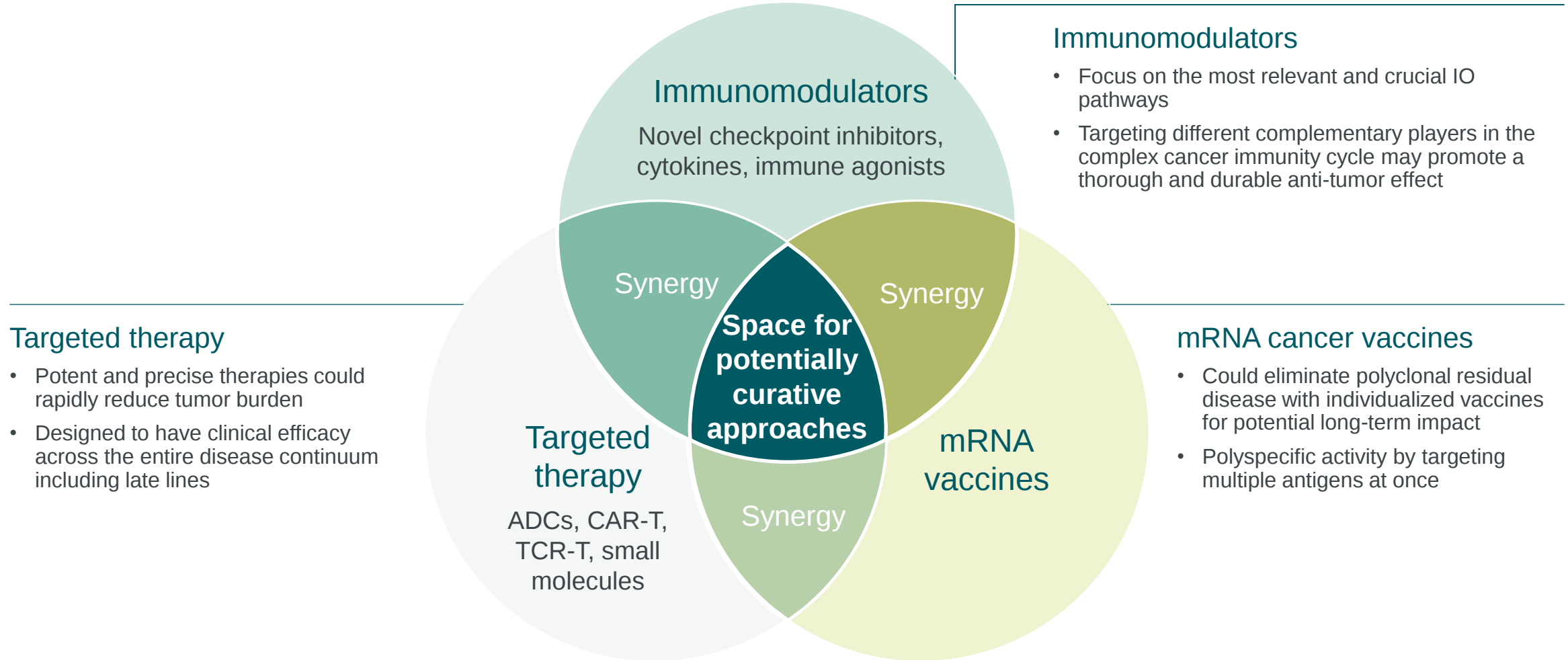
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This Slide Presentation Includes Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the rate and degree of market acceptance of BioNTech's investigational medicines, if approved; the initiation, timing, progress, results, and cost of BioNTech's research and development programs, including BioNTech's current and future preclinical studies and clinical trials, including statements regarding the timing of initiation, enrollment, and completion of studies or trials and related preparatory work and the availability of results, and the timing and outcome of applications for regulatory approvals and marketing authorizations; BioNTech's expectations regarding potential future commercialization in oncology, including goals regarding timing and indications; the targeted timing and number of additional potentially registrational trials, and the registrational potential of any trial BioNTech may initiate; discussions with regulatory agencies; BioNTech's expectations with respect to intellectual property; the impact of BioNTech's collaboration and licensing agreements; the development, nature and feasibility of sustainable vaccine production and supply solutions; and BioNTech's estimates of revenues, research and development expenses, selling, general and administrative expenses, and capital expenditures for operating activities. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words.

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Towards a Potentially Curative Approach to Cancer based on Multiple Modalities and Differentiated Novel/Novel Therapeutic Combinations



Our Multi-modality Immuno-Oncology Pipeline Today

Phase 1	Phase 1/2	Phase 2	Phase 3
BNT116 Adv. NSCLC	BNT142 (CD3xCLDN6) Multiple CLDN6-pos. adv. solid tumors	BNT111⁶ aPD-(L)1-R/R melanoma, + cemiplimab	BNT316/ONC-392 (gotistobart)⁴ (CTLA-4) aPD-(L)1 experienced NSCLC
Autogene cevumeran (BNT122)¹ Multiple solid tumors	BNT311/GEN1046 (acasunlimab)² (PD-L1x4-1BB) Multiple solid tumors	BNT113 1L rel./met. HPV16+ PDL-1+ head and neck cancer, + pembrolizumab	BNT323/DB-1303⁵ (HER2) HR+/HER2-low met. breast cancer
BNT152 + BNT153 (IL-7, IL-2) Multiple solid tumors	BNT312/GEN1042² (CD40x4-1BB) Multiple solid tumors	BNT116⁶ 1L adv. PD-L1 ≥ 50% NSCLC, + cemiplimab	
BNT211 (CLDN6) Multiple solid tumors	BNT314/GEN1059² (EpCAMx4-1BB) Multiple solid tumors	Autogene cevumeran (BNT122)¹ 1L adv. melanoma, + pembrolizumab	
BNT221 Refractory metastatic melanoma	BNT315/GEN1055² (OX40) Multiple solid tumors	Autogene cevumeran (BNT122)¹ Adj. ctDNA+ stage II or III CRC	
BNT321 (sLea) Metastatic PDAC	BNT316/ONC-392 (gotistobart)⁴ (CTLA-4) mCRPC, + radiotherapy	Autogene cevumeran (BNT122)¹ Adj. PDAC, + atezolizumab + mFOLFIRINOX	
BNT322/GEN1056² Multiple solid tumors	BNT316/ONC-392 (gotistobart)⁴ (CTLA-4) Multiple solid tumors	BNT311/GEN1046 (acasunlimab)² (PD-L1x4-1BB) R/R met. NSCLC, +/- pembrolizumab	
BNT326/YL202³ (HER3) Multiple solid tumors	BNT321 (sLeA) adjuvant PDAC, +mFOLFIRINOX	BNT316/ONC-392 (gotistobart)⁴ (CTLA-4) Plat.-R. ovarian cancer, + pembrolizumab	
	BNT323/DB-1303⁵ (HER2) Multiple solid tumors	BNT327/PM8002⁷ (PD-L1 x VEGF-A) 1L/2L+ ES-SCLC, +chemotherapy	
	BNT324/DB-1311⁵ (B7H3) Multiple solid tumors	BNT327/PM8002⁷ (PD-L1 x VEGF-A) 1L/2L met. TNBC, +chemotherapy	
	BNT325/DB-1305⁵ (TROP2) Multiple solid tumors		
	BNT327 / BNT325 combination^{7,5} Multiple solid tumors		

Legend

mRNA

Cell therapy

Next generation IO

ADCs

Novel combination studies

1. Partnered with Genentech, member of Roche Group; 2. Partnered with Genmab; 3. Partnered with MediLink Therapeutics; 4. Partnered with OncoC4; 5. Partnered with DualityBio; 6. Trials jointly conducted with Regeneron; 7. Partnered with Biotheus.

BioNTech at ESMO 2024 (1/2)

Modality	Program	Type Code	Title	Date, Time & Location
mRNA therapeutic vaccines	BNT113	Poster 877P	Exploratory efficacy and translational results from the safety run in of AHEAD-MERIT, a phase II trial of first line pembrolizumab plus the fixed-antigen cancer vaccine BNT113 in advanced HPV16+ HNSCC	- Sat, 14.09.2024 - Hall 6
	BNT113	Mini-oral 27LO	HARE-40: A phase I/II trial of therapeutic HPV vaccine (BNT113) in patients with HPV16 driven carcinoma	- Mon, 16.09.2024 11:15 - 11:20 AM CEST - Granada Auditorium - Hall 6
Cell therapies	BNT211	Proffered paper (10 min presentation) 611O	BNT211-01 (NCT04503278), an ongoing, first-in-human, Phase 1 study evaluating safety and efficacy of CLDN6 CAR T cells and a CLDN6-encoding mRNA vaccine in patients with relapsed/refractory CLDN6+ solid tumors	- Sun, 15.09.2024 15:45 - 15:55 PM CEST - Salamanca Auditorium - Hall 5

BioNTech at ESMO 2024 (2/2)

Modality	Program	Type Code	Title	Date, Time & Location
Protein-based Therapeutics	BNT323 / DB-1303¹	TiP 436TiP	DYNASTY-Breast02: A Phase 3 trial of BNT323/DB-1303 vs investigator's choice chemotherapy in HER2-low, hormone receptor positive, metastatic breast cancer	- Mon, 16.09.24 - Granada Auditorium - Hall 6
	BNT314 / GEN1059²	TiP 1072TiP	Phase 1/2 dose escalation/expansion trial to evaluate safety and preliminary efficacy of DuoBody-EpCAMx4-1BB (BNT314/GEN1059) alone or in combination with an immune checkpoint inhibitor in patients with malignant solid tumors	- Sat, 14.09.2024 - Granada Auditorium - Hall 6
	BNT316 / ONC-392³	LBA LBA32	A randomized, Phase 2, dose optimization of gotistobart, a pH-sensitive anti-CTLA-4, in combination with standard dose pembrolizumab in platinum-resistant recurrent ovarian cancer: safety, efficacy and dose optimization (PRESERVE-004/GOG-3081)	- Sun, 15.09.24 08:30 – 10:00 AM CEST - Burgos Auditorium – Hall 5
	BNT327 / PM8002⁴	Mini-oral 1255MO	A Phase II safety and efficacy study of PM8002/BNT327 in combination with chemotherapy in patients with EGFR-mutated non-small cell lung cancer (NSCLC)	- Sat, 14.09.2024 10:25 - 10:30 AM CEST - Santander Auditorium - Hall 5
	BNT327 / PM8002⁴	Mini-oral 348MO	A Phase Ib/II study to assess the safety and efficacy of PM8002/BNT327 in combination with nab-paclitaxel for first line treatment of locally advanced or metastatic triple-negative breast cancer	- Mon, 16.09.2024 08:35 - 08:40 AM CEST - Barcelona Auditorium - Hall 2
	BNT327 / PM8002⁴	Poster 1692P	A Phase Ib/IIa trial to evaluate the safety and efficacy of PM8002/ BNT327, a bispecific antibody targeting PD-L1 and VEGF-A, as a monotherapy in patients with advanced renal cell carcinoma	- Sun, 15.09.2024 - Granada Auditorium - Hall 6

1

BNT327 / PM8002¹ EGFR-mutated Non-Small Cell Lung Cancer

A Phase II Safety and Efficacy Study of PM8002/BNT327 in Combination with Chemotherapy in Patients with EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)

Yi-Long Wu, MD, (Lung Cancer Institute, Guangdong Province People's Hospital, Guangzhou, China) et al., Presentation Number: 1255MO

1. Partnered with Biotheus Inc.

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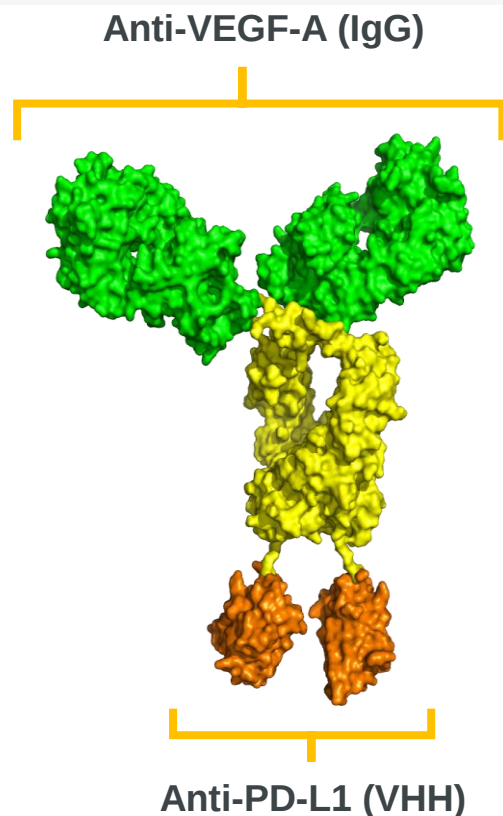
BNT327/PM8002¹ – A Next-Gen IO Agent that Combines Two Clinically Validated MoAs

Dual blockade of PD-L1 and VEGF-A has demonstrated clinical synergy

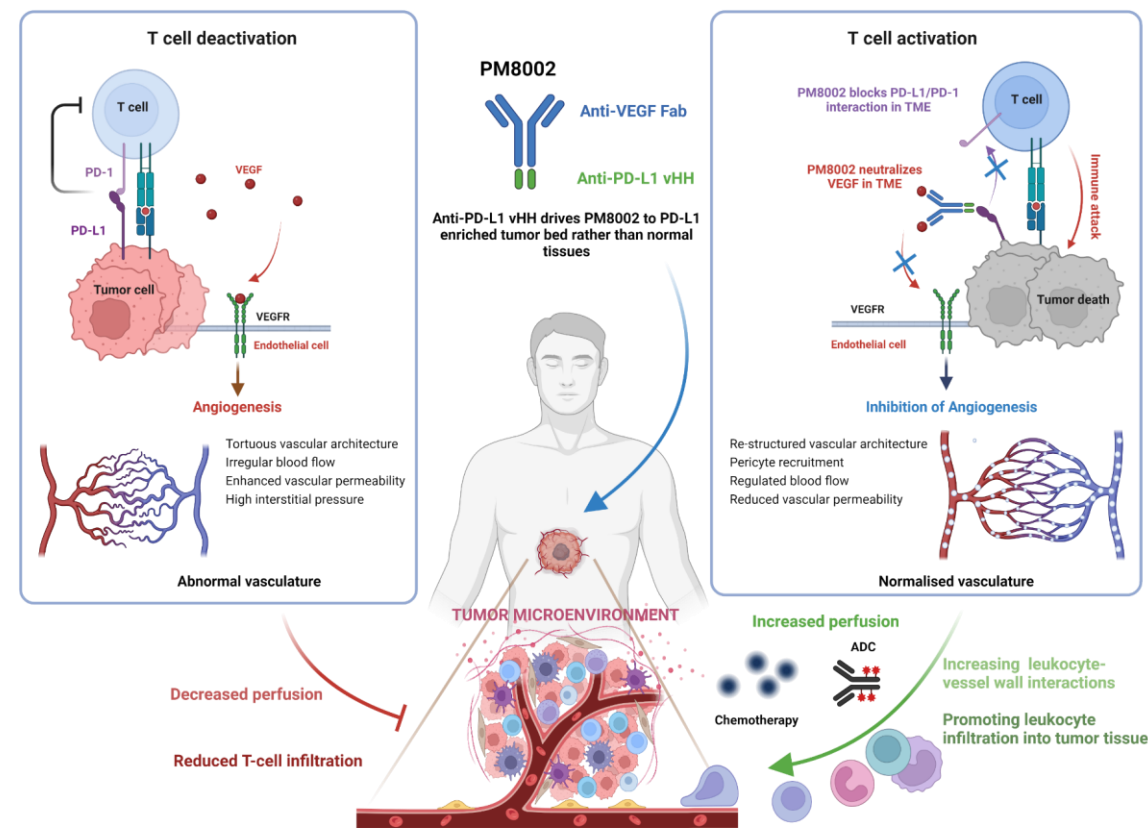
- Compelling profile with over 600 patients treated to date
- Monotherapy activity and synergy in combination therapy observed in early clinical studies
- Encouraging safety profile vs. PD-L1 + VEGF inhibition or PD-1 alone

Protein binding activity (K_D) for human

- PD-L1: 5.5 nM
- VEGF-A: <0.4 nM



“Two in one” mechanism-of-action synergizes with ADCs



1. Partnered with Biotheus Inc. ADC = antibody drug conjugate; IgG = immunoglobulin G; IO = immuno-oncology; MoA = Mechanism of Action; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; TME = tumor microenvironment; VEGF = vascular endothelial growth factor; VHH = heavy chain variable. The mechanism of action graphic was generated by Biorender.com.

BNT327/PM8002¹ in Combination with Chemotherapy in Patients with Advanced NSCLC

Multicenter, single arm, Phase 2 study to evaluate efficacy and safety of BNT327/PM8002 in combination with chemotherapy in patients with advanced NSCLC ([NCT05756972](#))

Inclusion criteria

- Age ≥ 18 years
- Nonsquamous Stage IIIB/C and IV NSCLC ineligible for surgery or local therapy
- EGFR sensitizing mutation
- Failure of EGFR-TKI treatment(s)
- No other prior systemic therapy than EGFR-TKIs
- Asymptomatic/stable brain metastasis allowed

N=64

**BNT327/PM8002¹, 30 mg/kg +
Carboplatin, AUC 5 mg/ml/min +
Pemetrexed, 500 mg/m²
Q3W for 4 cycles**

**BNT327/PM8002¹, 30 mg/kg +
Pemetrexed, 500 mg/m²
Maintenance Q3W**

Analysis by PD-L1 expression was determined with immunohistochemistry and classified based on tumor proportion score (TPS).

All biopsies were taken after progression on EGFR-TKI therapy.



Endpoints

Primary:

ORR (assessed by investigator per RECIST 1.1)

1. Partnered with Biotheus, Inc.

CTx = chemotherapy; ECOG = Eastern Cooperative Oncology Group; mEGFR = mutated epidermal growth factor receptor; NSCLC = non-small cell lung cancer; ORR = objective response rate; QxW = every x weeks; RECIST = Response Evaluation Criteria in Solid Tumors; SoC = standard of care; TKI = tyrosine kinase inhibitor.

Baseline Characteristics

	Overall n=64	PD-L1 negative (TPS<1%) n=28	PD-L1 low expression (TPS 1 to 49%) n=23	PD-L1 high expression (TPS ≥ 50%) n=13
Median age, years (range)	59.5 (32,76)	59.0 (36,76)	59.6 (44,75)	60.2 (32,74)
Female, n (%)	29 (45.3)	11 (39.3)	11 (47.8)	7 (53.8)
Brain metastasis, n (%)	15 (23.4)	7 (25.0)	5 (21.7)	3 (23.1)
Liver metastasis, n (%)	11 (17.2)	5 (17.9)	5 (21.7)	1 (7.7)
EGFR mutation, n (%)				
19Del	32 (50.0)	10 (35.7)	15 (65.2)	7 (53.8)
L858R	29 (45.3)	17 (60.7)	7 (30.4)	5 (38.5)
Others*	3 (4.7)	1 (3.6)	1 (4.4)	1 (7.7)
T790M status, n (%)				
Negative	39 (60.9)	19 (67.9)	15 (65.2)	5 (38.5)
Positive	12 (18.8)	6 (21.4)	4 (17.4)	2 (15.4)
Unknown	13 (20.3)	3 (10.7)	4 (17.4)	6 (46.2)
Previous EGFR-TKI treatment, n (%)				
1 st /2 nd Gen TKI only	5 (7.8)	3 (10.7)	0 (0)	2 (15.4)
3 rd Gen TKI only	41 (64.1)	17 (60.7)	16 (69.6)	8 (61.5)
1 st /2 nd Gen TKI, then 3 rd Gen TKI	18 (28.1)	8 (28.6)	7 (30.4)	3 (23.1)

*others: S768I, L861Q, G719X

Cut-off date: July 24, 2024

1. Partnered with Biotheus, Inc.
EGFR = epidermal growth factor receptor; Gen = generation; TKI = tyrosine kinase inhibitor;

BNT327/PM8002¹ Showed Anti-Tumor Activity Independent of PD-L1 Expression Levels

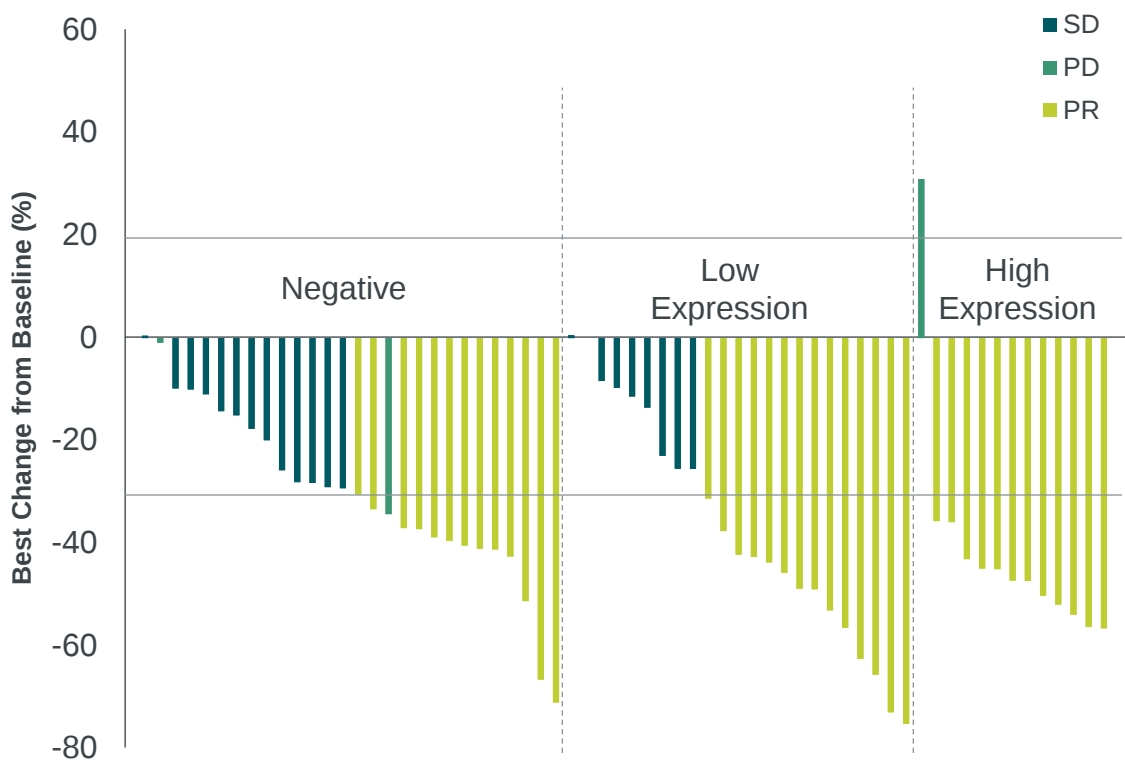
Response Assessment	Overall n=64	PD-L1 negative n=28	PD-L1 low expression n=23	PD-L1 high expression n=13
ORR by investigator, n (%) [95% CI]	39 (60.9) [47.9, 72.9]	13 (46.4) [27.5, 66.1]	14 (60.9) [38.5, 80.3]	12 (92.3) [64.0, 99.8]
Confirmed ORR by investigator, n (%) [95% CI]	37 (57.8) [44.8, 70.0]	11 (39.3) [21.5, 59.4]	14 (60.9) [38.5, 80.3]	12 (92.3) [64.0, 99.8]
Best overall response, n (%)				
PR	37 (57.8)	11 (39.3)	14 (60.9)	12 (92.3)
SD	24 (37.5)	15 (53.6)	9 (39.1)	0 (0)
PD	3 (4.7)	2 (7.1)	0 (0)	1 (7.7)
DCR, n (%) [95% CI]	61 (95.3) [86.9, 99.0]	26 (92.9) [76.5, 99.1]	23 (100) [85.2, 100.0]	12 (92.3) [64.0, 99.8]
Median TTR, months [95% CI]	2.9 [1.5, 4.1]	5.8 [2.7, NE]	2.9 [1.4, NE]	1.6 [1.5, 2.9]

Cut-off date: July 24, 2024
Median follow-up time: 7.7 months

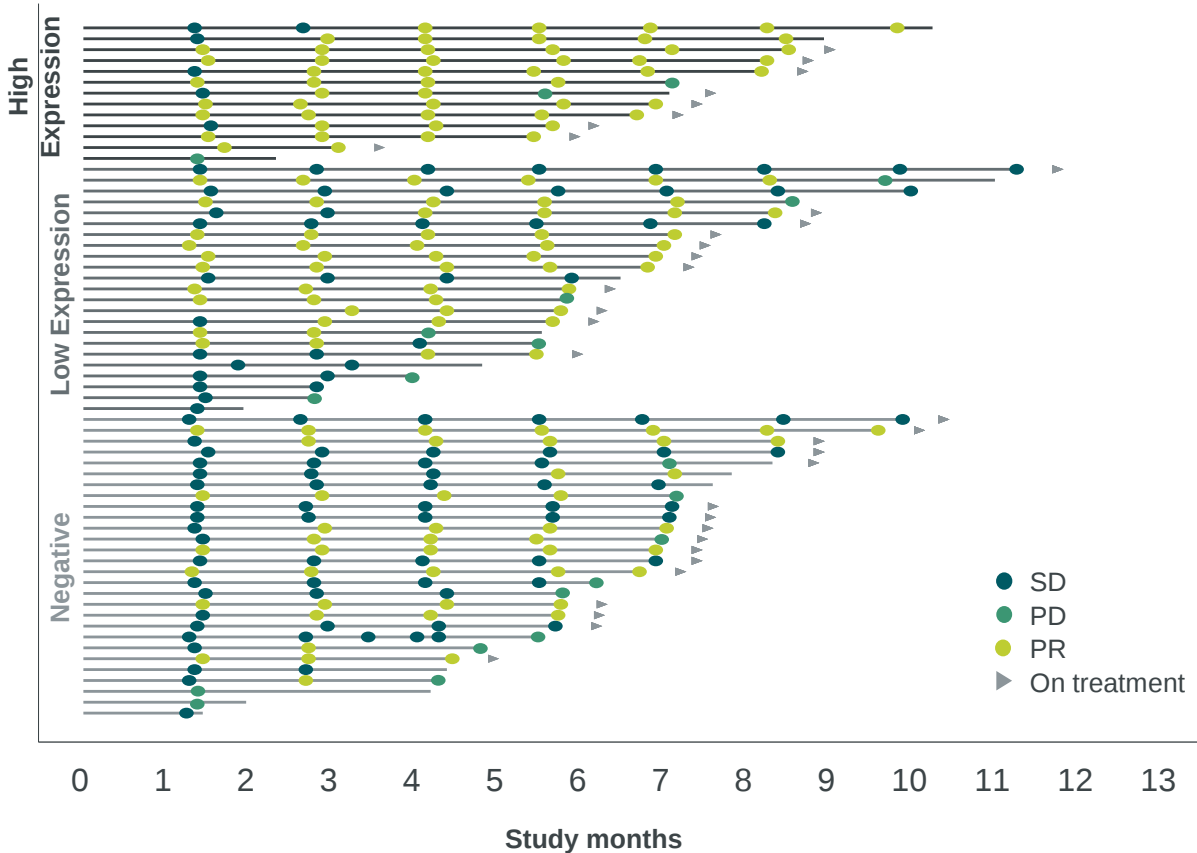
1. Partnered with Biotheus Inc.
CI = confidence interval; DCR = disease control rate; NE = not evaluable.; ORR = objective response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; TTR = time to response.

BNT327/PM8002¹ Showed Positive Correlation Between Higher Tumor PD-L1 Expression Levels and Overall Response Rates

Waterfall plot of best change of target lesions from baseline for patients grouped by PD-L1 expression



Swimmer plot of treatment duration for patients grouped by PD-L1 expression



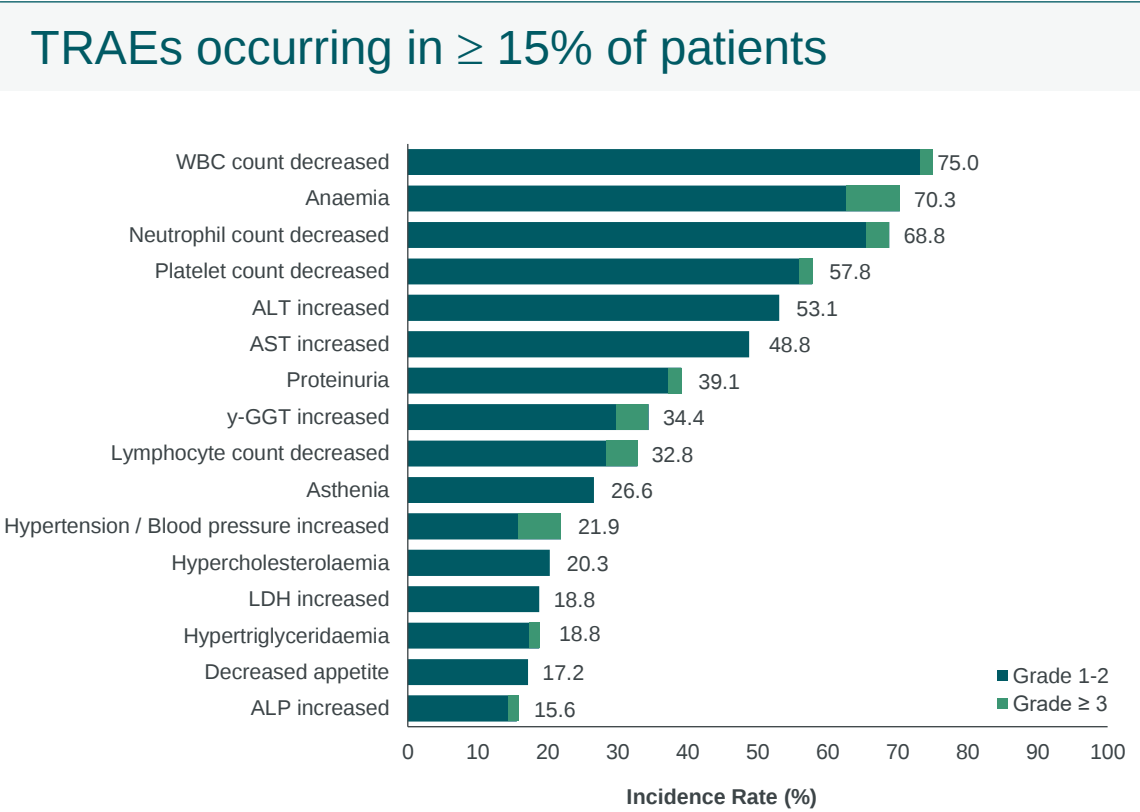
Median follow-up time: 7.7 months

1. Partnered with Biotheus Inc.,
PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease.

BNT327/PM8002¹ Shows Generally Manageable Safety Profile

Safety summary	
	Overall (n=64)
Any TEAE, n (%)	64 (100)
Grade ≥3	45 (70.3)
Any TRAE, n (%)	63 (98.4)
Grade ≥3	39 (60.9)
Leading to interruption of PM8002/BNT327	20 (31.3)
Leading to discontinuation of only PM8002/BNT327	4 (6.3)
Leading to discontinuation of only chemotherapy	4 (6.3)
Leading to discontinuation of PM8002/BNT327 and chemotherapy	1 (1.6)
Leading to death [#]	1 (1.6)
Any-grade immune-related	26 (40.6)
Grade ≥3 immune-related	4 (6.3)
Grade ≥3 VEGF-related [*]	7 (10.9)
SAE	11 (17.2)

[#]TRAE leading to death: 1 case of pneumonia.
^{*}Grade ≥3 VEGF-related TRAEs included hypertension/elevated blood pressure, proteinuria, epistaxis, hemoptysis.



Cut-off date: July 24, 2024
Median follow-up time: 7.7 months

Only low rate of treatment discontinuation due to TRAEs

1. Partnered with Biotheus Inc; ALP = Alkaline phosphatase.; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; LDH, Lactate dehydrogenase; SAE = serious adverse event (related to any drug); TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event (related to any drug); WBC = White blood cell; γ-GGT = Gamma-glutamyltransferase;.

BNT327/PM8002¹ (EGFRmut NSCLC) – ESMO 2024 Data: Key Takeaway Messages



Efficacy

BNT327/PM8002¹ plus chemotherapy showed encouraging antitumor activity in patients with EGFR-mutated NSCLC who progressed on prior EGFR-TKI treatment(s).

The anti-tumor activity of BNT327/PM8002¹ therapy was observed independent of PD-L1 expression levels (PD-L1 negative NSCLC showed 39.3% cORR), with a positive correlation seen between higher tumor PD-L1 expression levels and overall response rates.



Safety Profile

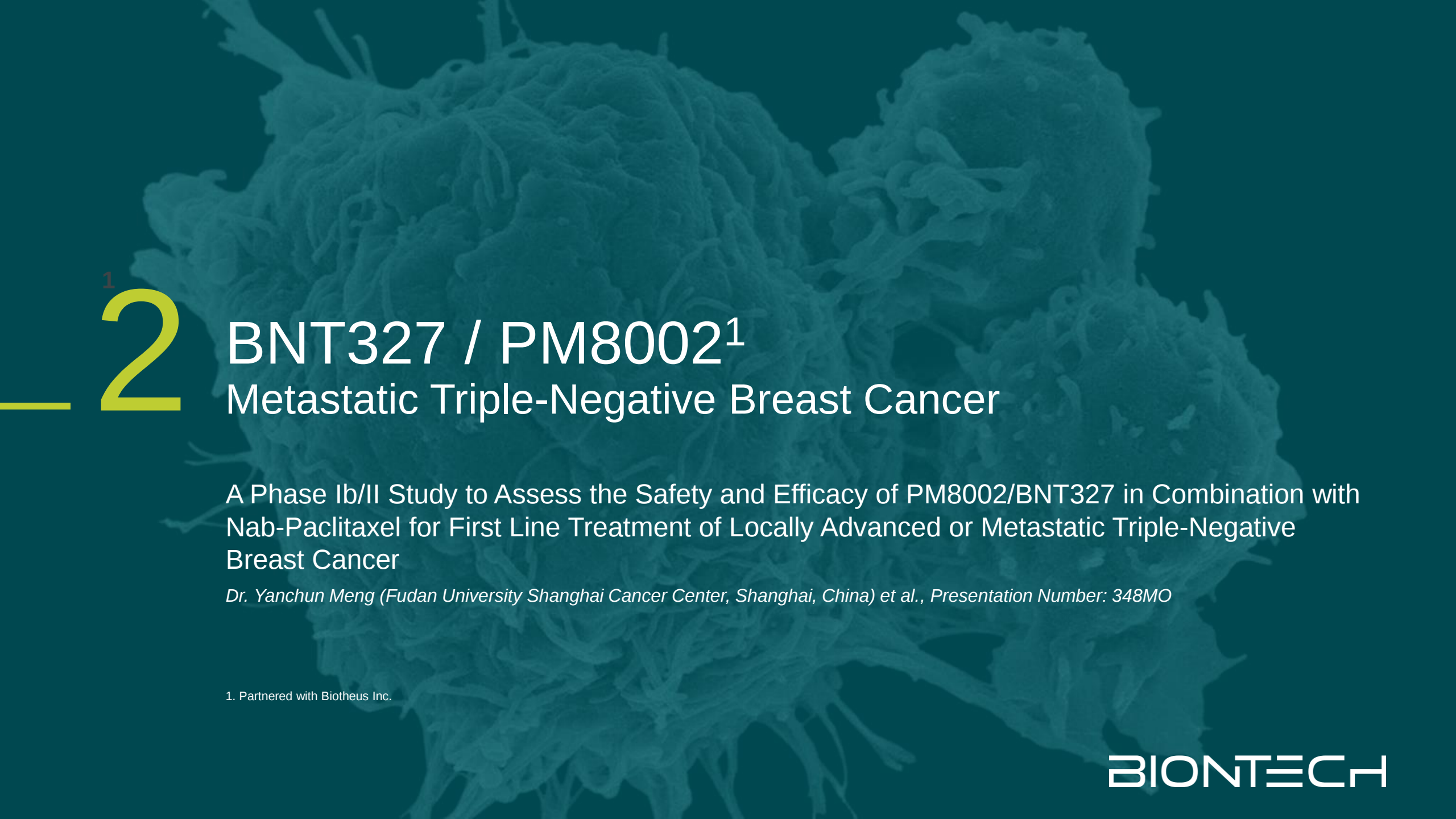
The safety profile was generally manageable, with a low rate of treatment discontinuation.



Outlook

Based on these findings, further clinical trials in NSCLC are warranted.

1. Partnered with Biotheus Inc.; EGFRmut = mutated epidermal growth factor receptor; NSCLC = non-small cell lung cancer; cORR = confirmed objective response rate; PD-L1 = programmed cell death ligand 1.



1
2

BNT327 / PM8002¹

Metastatic Triple-Negative Breast Cancer

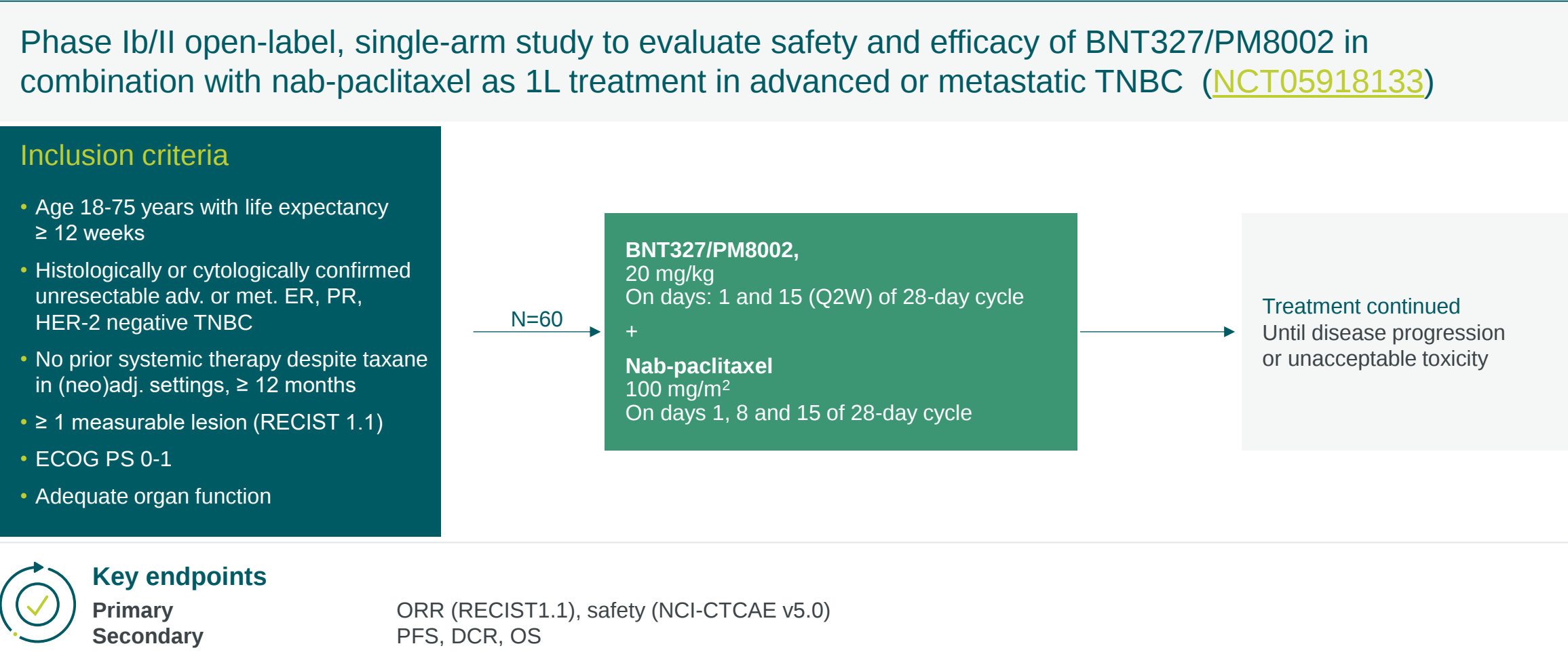
A Phase Ib/II Study to Assess the Safety and Efficacy of PM8002/BNT327 in Combination with Nab-Paclitaxel for First Line Treatment of Locally Advanced or Metastatic Triple-Negative Breast Cancer

Dr. Yanchun Meng (Fudan University Shanghai Cancer Center, Shanghai, China) et al., Presentation Number: 348MO

1. Partnered with Biotheus Inc.

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BNT327/PM8002¹ in Combination with Nab-Paclitaxel as First Line Treatment for Patients with Metastatic TNBC



1. Partnered with Biotheus, Inc. ; 1L = first line; DCR = disease control rate; DOR = durability of response; ECOG PS= eastern cooperative oncology group performance status; ER = estrogen receptor; HER-2 = human epidermal growth factor receptor 2; NCI-CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; ORR = Overall response rate; OS = overall survival; PFS = progression free survival; PR = progesterone receptor; Q2W = every two weeks; RECIST = Response Evaluation Criteria in Solid Tumors; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

Baseline Characteristics

Study status

As of July 05, 2024, **42 patients had been enrolled** and received at least 1 dose of BNT327/ PM8002 combined with nab-paclitaxel

11 pts remained on treatment

Median follow-up time 16.3 months

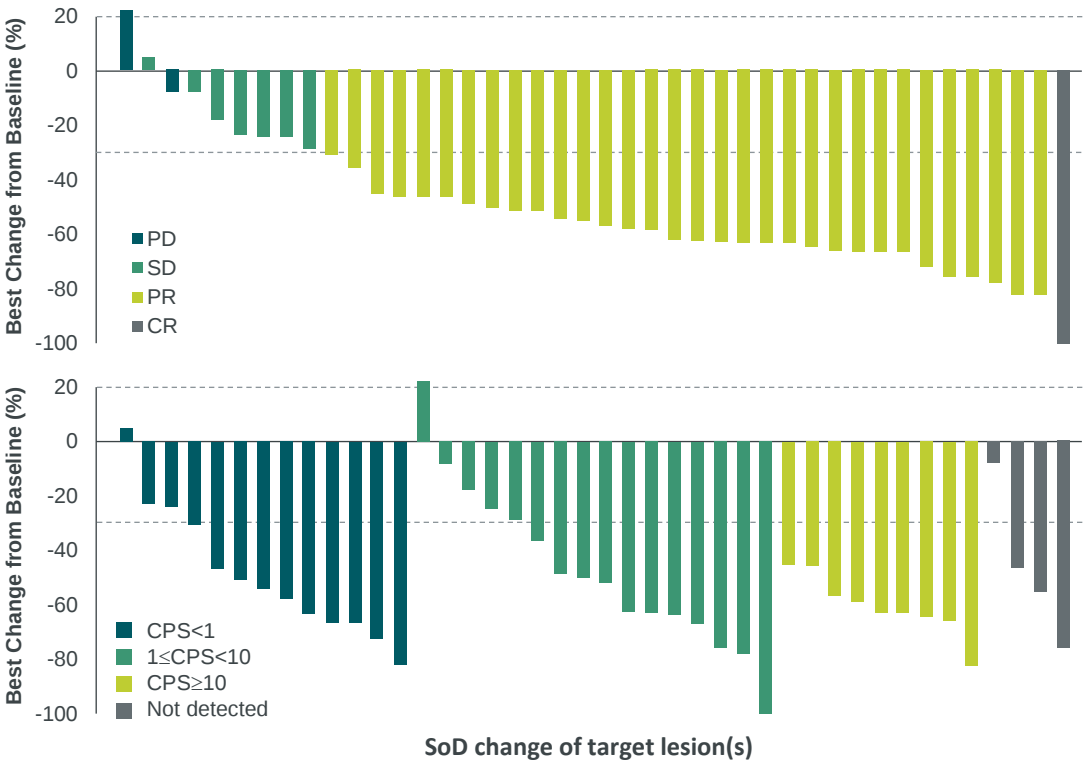
Patient Characteristics (n=42)

Median age, years (Q1, Q3)	53.5 (41.0, 60.0)
Number of metastatic sites, n (%)	
0-2	17 (40.5)
≥ 3	25 (59.5)
Liver metastasis, n (%)	
Yes	16 (38.1)
No	26 (61.9)
Brain metastasis, n (%)	
Yes	2 (4.8)
No	40 (95.2)
Neo/adjuvant Paclitaxel treatment, n (%)	
Yes	28 (66.7)
No	14 (33.3)

Partnered with Biotheus Inc.;
irAEs = immune-related adverse events; SAEs = severe adverse events; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

BNT327/PM8002¹ Showed Clinically Meaningful Efficacy irrespective of PD-L1 status

Variable	ITT	PD-L1 CPS<1	PD-L1 1≤CPS<10	PD-L1 CPS≥10	Not detected
Population (n)	42	13	16	9	4
CR	1 (2.4)	0 (0.0)	1 (6.3)	0 (0.0)	0 (0.0)
PR	32 (76.2)	10 (76.9)	10 (62.5)	9 (100.0)	3 (75.0)
SD	7 (16.7)	3 (23.1)	4 (25.0)	0 (0.0)	0 (0.0)
PD	2 (4.8)	0 (0.0)	1 (6.3)	0 (0.0)	1 (25.0)
ORR % (95% CI)	78.6 (63.2, 89.7)	76.9 (46.2, 95.0)	68.8 (41.3, 89.0)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
cORR % (95% CI)	73.8 (58.0, 86.1)	76.9 (46.2, 95.0)	56.3 (29.9, 80.3)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
DCR % (95% CI)	95.2 (83.8, 99.4)	100.0 (75.3, 100.0)	93.8 (69.8, 99.8)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
mPFS (Mo), (95%CI)	13.5 (9.4, --)	NR (5.7, --)	14.0 (7.2, --)	10.8 (5.5, 13.5)	14.0 (1.8, --)



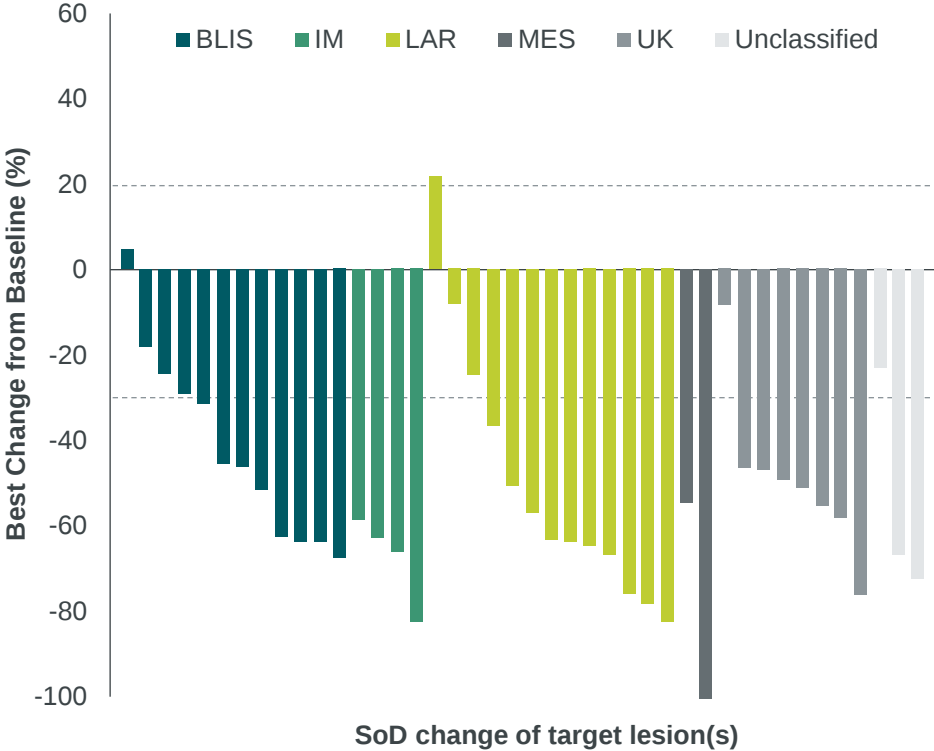
For the ITT population, mTTR was 1.9 mo and mDoR 11.7 mo; mOS was not reached

PD-L1 status was assessed by means of the PD-L1 IHC E1L3N assay

1. Partnered with Biotheus Inc.; CPS = combined positive score; CR = complete response; cORR = confirmed ORR; DCR = disease control rate; IHC = immunohistochemistry; ITT = intention to treat; mDoR = median duration of response; mOS = median overall survival; mPFS = median progress-free survival; mTTR = median time to response; ORR = objective response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; SoD = sum of diameters

BNT327/PM8002¹ Showed Similar ORR Regardless of FUDAN Type

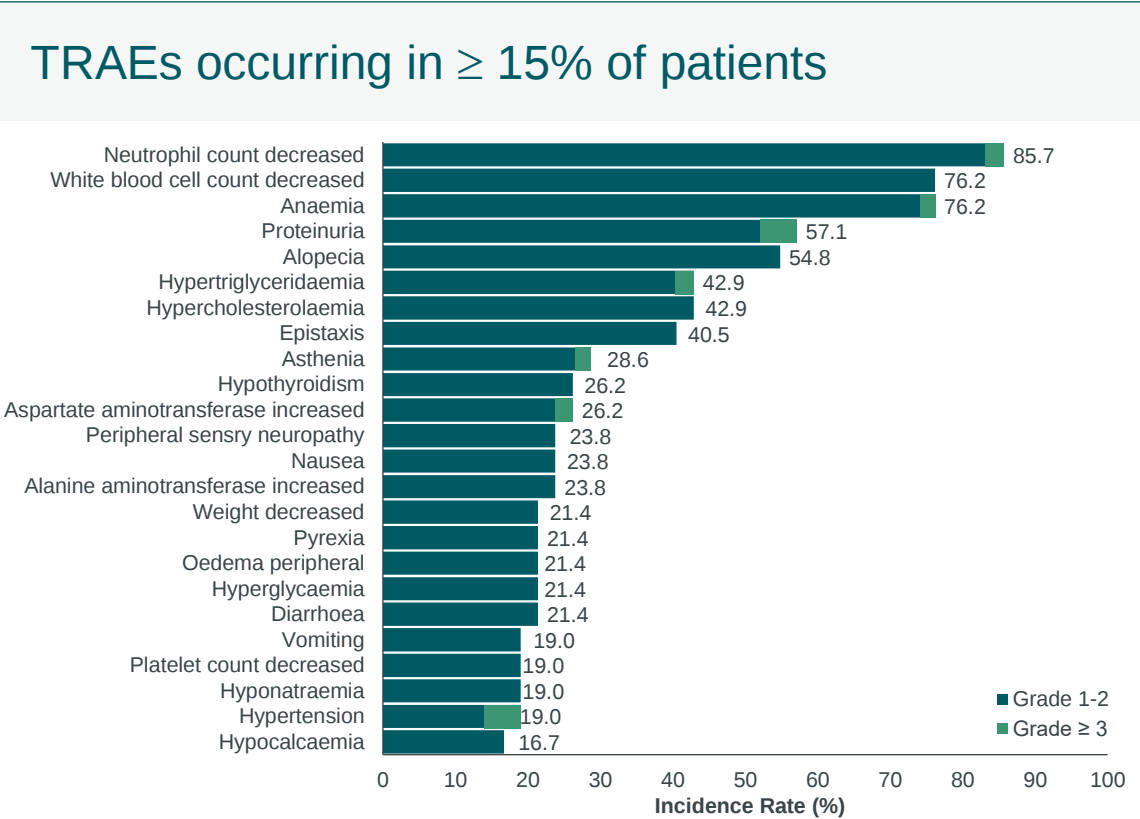
Variable	BLIS	IM	LAR	MES	Unclassified	Unknown
Population (n)	12	4	13	2	3	8
CR	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)
PR	8 (66.7)	4 (100.0)	10 (76.9)	1 (50.0)	2 (66.7)	7 (87.5)
SD	4 (33.3)	0 (0.0)	2 (15.4)	0 (0.0)	1 (33.3)	0 (0.0)
PD	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)	1 (12.5)
ORR, % (95% CI)	66.7 (34.9, 90.1)	100.0 (39.8, 100.0)	76.9 (46.2, 95.0)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
cORR, % (95% CI)	58.3 (27.7, 84.8)	100.0 (39.8, 100.0)	69.2 (38.6, 90.9)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
DCR % (95% CI)	100.0 (73.5, 100.0)	100.0 (39.8, 100.0)	92.3 (64.0, 99.8)	100.0 (15.8, 100.0)	100.0 (29.2, 100.0)	87.5 (47.3, 99.7)



1. Partnered with Biotheus Inc.; BLIS = basal-like and immune-suppressed; CR = complete response; cORR = confirmed ORR; DCR = disease control rate; FUDAN Type = molecular subtype classification determined by IHC analysis, developed by Fudan University Shanghai Cancer Center; IM = immunomodulatory; LAR = luminal androgen receptor; mDoR = median duration of response; MES = mesenchymal-like; mPFS = median progress-free survival; mTTR = median time to response; ORR = objective response rate; PD = progressive disease; PR = partial response; SD = stable disease; SoD = sum of diameters; UK = unknown

BNT327/PM8002¹ Showed Manageable Safety Profile in Patients with TNBC

Safety summary	
Safety Overview	N=42 n (%)
All TRAEs	42 (100)
Grade ≥3 TRAEs	24 (57.1)
SAEs	10 (23.8)
TRAE leading to dose interruption	27 (64.3)
TRAE leading to dose reduction	7 (16.7)
TRAEs leading to treatment discontinuation	2 (4.8)
irAE	15 (35.7)
Grade ≥3 irAE	4 (9.5)



Any-grade and grade ≥3 TRAEs of the combination regimen occurred in 100% and 57.1% patients, respectively TRAEs leading to treatment discontinuation occurred in 4.8% patients

1. Partnered with Biotheus Inc.; irAEs = immune-related adverse events; SAEs = severe adverse events; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

BNT327/PM8002¹ (mTNBC) – ESMO 2024 Data: Key Takeaway Messages



Efficacy

In patients with locally advanced/metastatic TNBC, first line treatment with BNT327/PM8002¹ + nab-paclitaxel is associated with:

- Rapid shrinkage of target lesions.
- Clinically meaningful antitumor activity regardless of PD-L1 status and FUDAN type.



Safety Profile

Manageable toxicity: No new safety signals were observed beyond those typically described for anti-PD-1/PD-L1 and anti-VEGF therapies and chemotherapy.



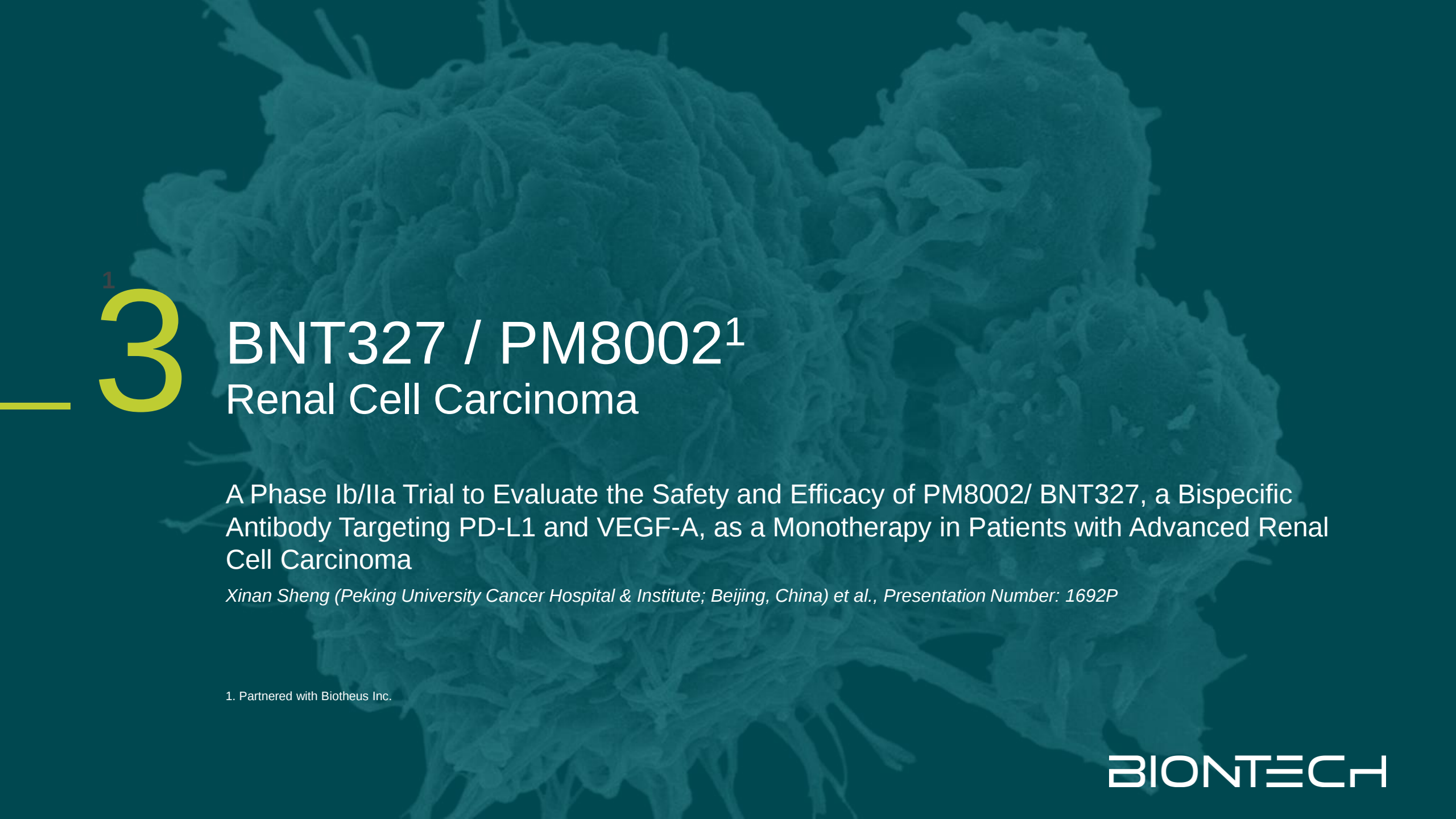
Outlook

Study limitations: single arm and small sample size.

BNT327/PM8002¹ shows a favorable safety profile and early signals of efficacy in first line treatment of TNBC which will be further explored in ongoing trials.

Phase III trial (NCT06419621) in China as well as global Phase II trial (NCT06449222) ongoing in TNBC.

1. Partnered with Biotheus Inc.;
FUDAN Type = molecular subtype classification determined by IHC analysis, developed by Fudan University Shanghai Cancer Center; mTNBC = metastatic triple negative breast cancer; PD-(L)1 = programmed cell death protein (ligand) 1;
VEGF = vascular epidermal growth factor;



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BNT327 / PM8002¹

Renal Cell Carcinoma

A Phase Ib/IIa Trial to Evaluate the Safety and Efficacy of PM8002/ BNT327, a Bispecific Antibody Targeting PD-L1 and VEGF-A, as a Monotherapy in Patients with Advanced Renal Cell Carcinoma

Xinan Sheng (Peking University Cancer Hospital & Institute; Beijing, China) et al., Presentation Number: 1692P

1. Partnered with Biotheus Inc.

BIONTECH

Trial Design of BNT327/PM8002¹ Monotherapy in Patients with Advanced Solid Tumors including 2L ccRCC and 1L nccRCC

Phase 1b/2a open-label multiple cohort, dose-expansion monotherapy study to evaluate safety and efficacy of BNT327/PM8002 in patients with advanced solid tumors, including RCC ([NCT05918445](#))

Inclusion criteria

- Age 18-75 years with life expectancy $\geq$ 12 weeks
- Locally advanced inoperable or metastatic RCC with or without sarcomatoid component
 - ccRCC: progress on prior 1L VEGF TKI +/- IO
 - nccRCC: no prior systemic therapy
- Malignant tumor confirmed by histology or cytology
- Adequate organ function
- $\geq$ 1 measurable lesion not been previously treated (RECIST 1.1)
- ECOG 0-1

N = 53

BNT327/PM8002, iv,
Q2W or Q3W

Treatment continued
until disease progression
or intolerable toxicity



Study endpoints

Primary:

Secondary:

ORR assessed by investigators per RECIST v1.1

DCR (RECIST v1.1), DOR (RECIST v1.1), PFS, safety

1. Partnered with Biotheus Inc.; ADA = anti-drug antibody; ccRCC = clear cell renal cell carcinoma; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; iv = intravenously; nccRCC = non-clear cell renal cell carcinoma; NCI-CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PK = pharmacokinetic parameters; QxW = every x weeks; RECIST = Response Evaluation Criteria in Solid Tumors; TRAE = treatment-related adverse event.

BNT327/PM8002¹ Phase 1b/2a Study in Patients with RCC – Baseline Characteristics

Study status

As of July 5, 2024, **31 patients with ccRCC** and **22 patients with nccRCC** had been enrolled.

A few patients had favorable-risk disease in both cohorts and majority of patients had intermediate or poor disease.

In the nccRCC cohort, the most common histologic subtype was papillary.

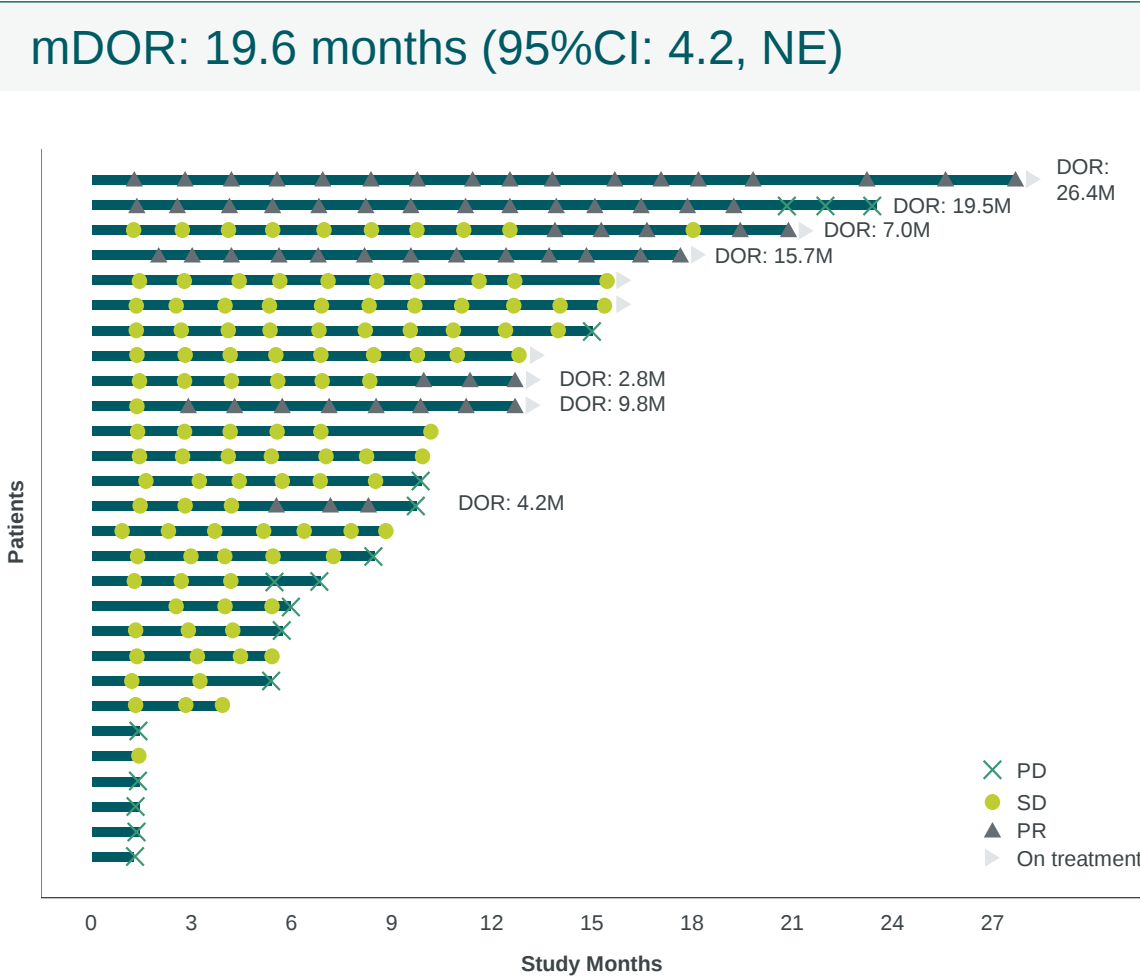
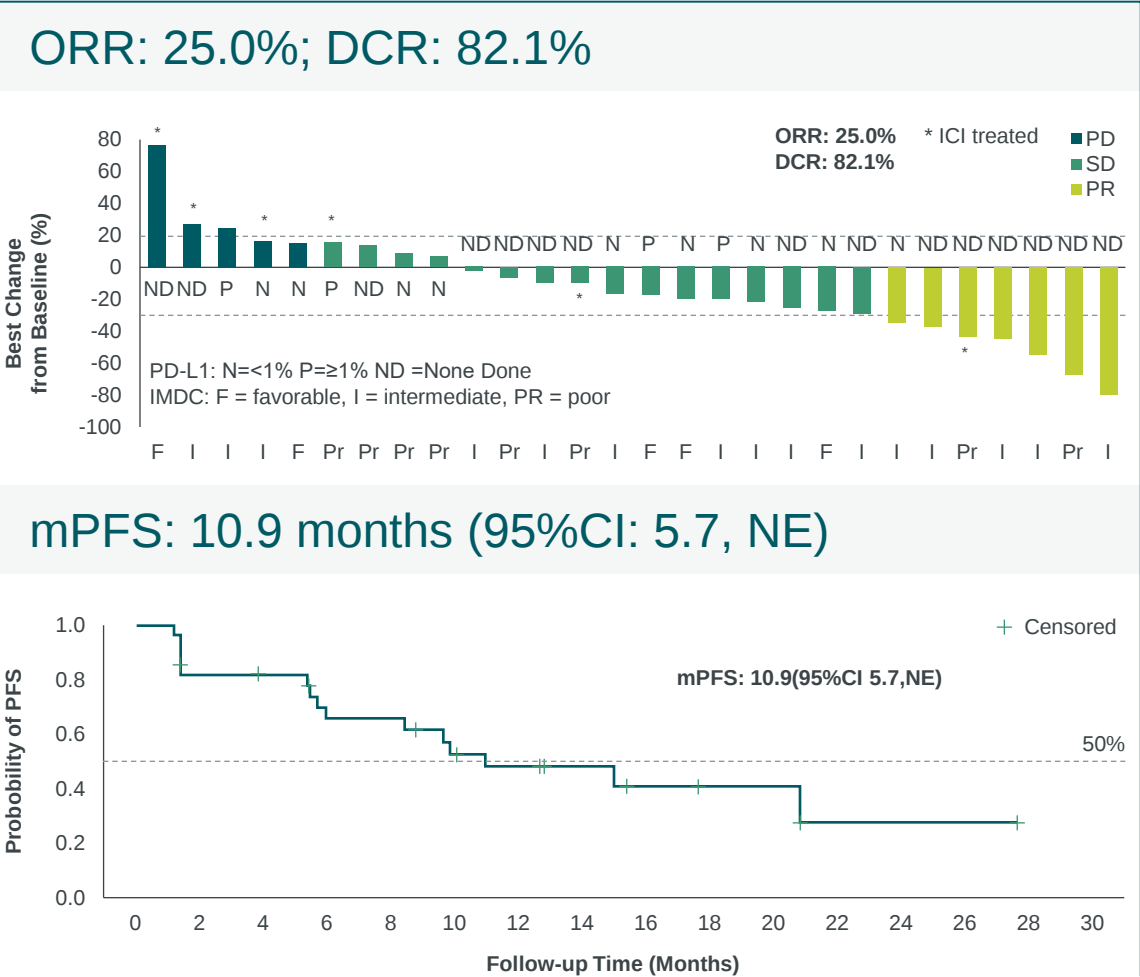
Median duration of follow-up was 14.1 months (0.9, 27.6) in ccRCC and 9.0 months (1.6, 26.9) in nccRCC.

Characteristics	2L ccRCC (n=31)	1L nccRCC (n=22)
Median age, years (Q1, Q3)	59.0 (54.0, 66.0)	53.5 (42.0, 62.0)
Sex, n (%)		
Male	20 (64.5)	16 (72.7)
Female	11 (35.5)	6 (27.3)
ECOG, n (%)		
0	12 (38.7)	10 (45.5)
1	19 (61.3)	12 (54.5)
IMDC risk group, n (%)		
Favorable	6 (19.4)	2 (9.1)
Intermediate/poor	25 (80.6)	20 (90.9)
PD-L1 CPS, n (%)		
<1%	9 (29.0)	3 (13.6)
≥1%	5 (16.1)	1 (4.6)
Not Done	17 (54.8)	18 (81.8)
Histology, n (%)		
Clear cell	31 (100)	0
Papillary	0	10 (45.5)
TFE3	0	4 (18.2)
FH-deficient	0	3 (13.6)
Other*	0	5 (22.7)
Prior systemic anticancer therapy, n (%)		
VEGF TKI only	25 (80.6)	0
VEGF TKI and prior ICIs	6 (19.4)	0
Previous nephrectomy, n (%)	21 (67.7)	15 (68.2)

1. Partnered with Biotheus Inc.; *Other included ESC RCC (n=2), translocation RCC (n=1), oncocytoma (n=1) and chromophobe (n=1).

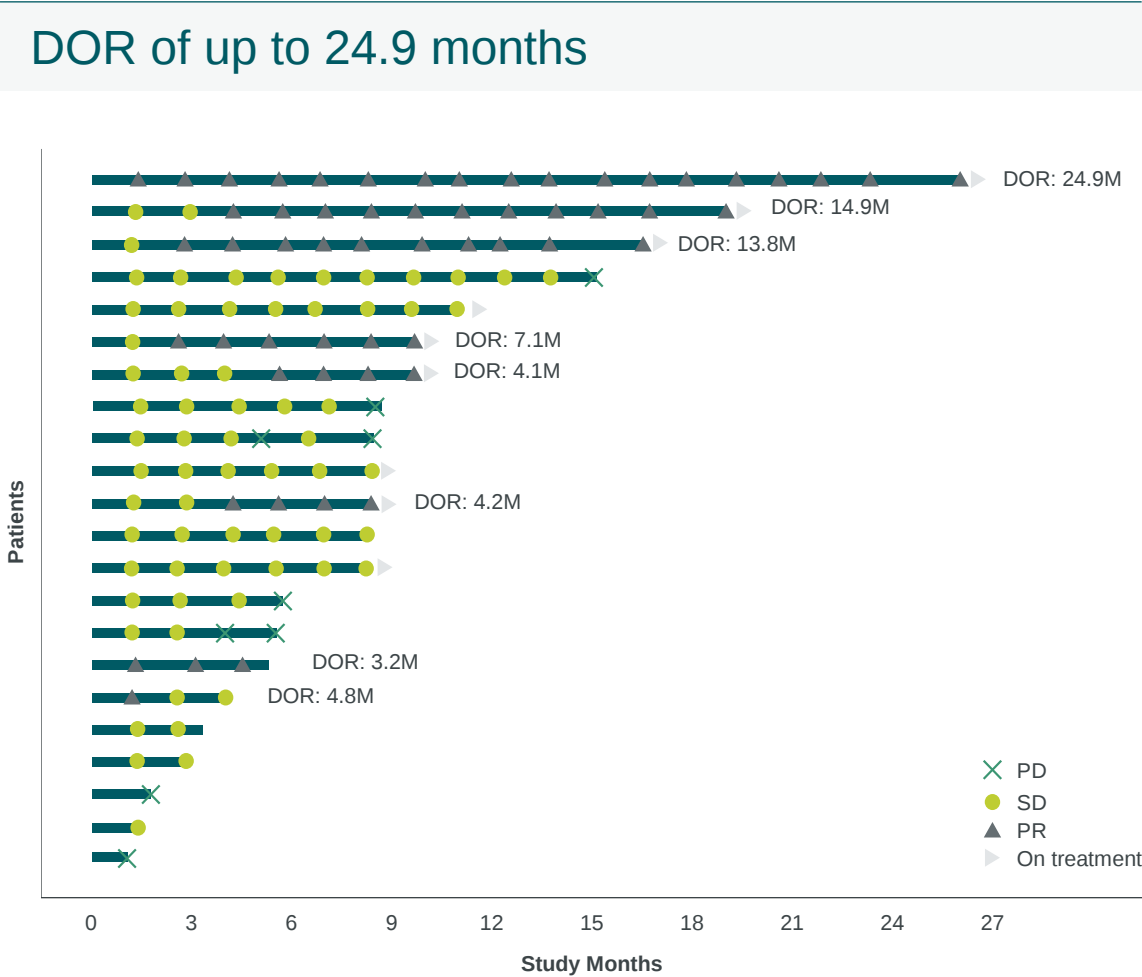
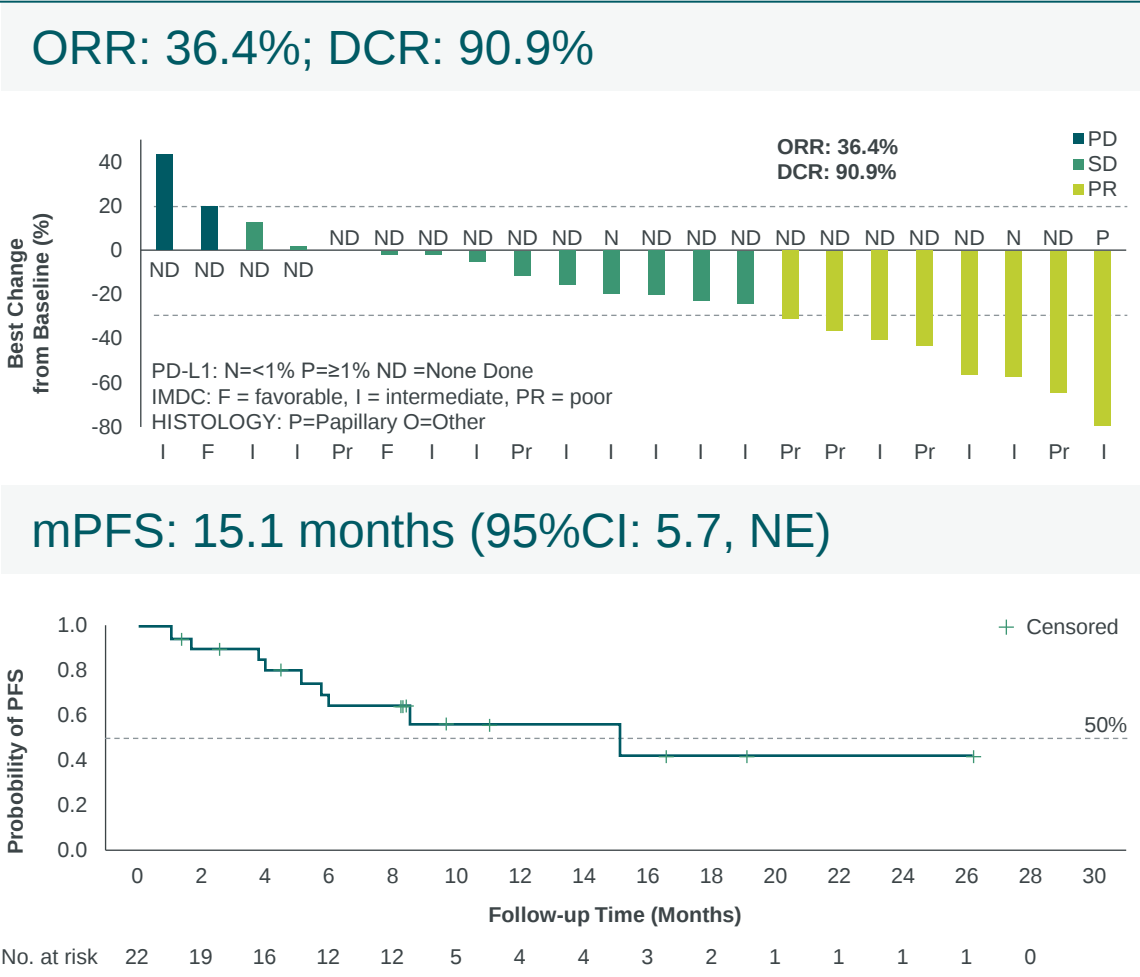
CPS = combined positive score; ECOG = Eastern Cooperative Oncology Group; FH = Fumarate hydratase; ICI = immune checkpoint inhibitor; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; (n)ccRCC = (non-) clear cell renal cell carcinoma; PD-L1 = programmed cell death ligand 1; TFE3 = RCC = renal cell carcinoma; VEGF TKI = Vascular endothelial growth factor tyrosine kinase inhibitors.

BNT327/PM8002¹ Showed Encouraging Anti-Tumor Activity in Patients with ccRCC (n = 28)



1. Partnered with Biotheus Inc.
ccRCC = clear cell renal cell carcinoma; CI = confidence interval; DCR = disease control rate; DOR = duration of response; ICI = immune checkpoint inhibitor; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease; NE = not evaluable.

BNT327/PM8002¹ Showed Encouraging Anti-Tumor Activity in Patients with nccRCC across subtypes (n = 22)



1. Partnered with Biotheus Inc.;
CI = confidence interval; DCR = disease control rate; DOR = duration of response; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; nccRCC = non-clear cell renal cell carcinoma; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease; NE = not evaluable.

BNT327/PM8002¹ Showed Manageable Safety in Patients with Advanced nccRCC or ccRCC

Safety observations

All patients experienced any-grade treatment-related adverse events (TRAEs).

Most AEs were Grades 1-2.

Categories	n (%)			
All TRAEs	53 (100)			
≥Grade 3 TRAEs	22 (41.5)			
irAEs	26 (49.1)			
SAEs	8 (15.1)			
TRAEs leading to discontinuation	1 (1.9)			
	Grade, n (%)			
TRAE ≥10%	All	3	4	5
Proteinuria	30 (56.6)	8 (15.1)	0	0
Hypertriglyceridaemia	16 (30.2)	2 (3.8)	0	0
Hypercholesterolaemia	15 (28.3)	0	0	0
Hypertension	11 (20.8)	8 (15.1)	0	0
Blood creatinine increased	10 (18.9)	0	0	0
Blood pressure increased	9 (17.0)	3 (5.7)	0	0
Low density lipoprotein increased	9 (17.0)	0	0	0
Apolipoprotein B increased	9 (17.0)	0	0	0
Blood cholesterol increased	8 (15.1)	0	0	0
Rash	8 (15.1)	0	0	0
Hypoalbuminaemia	8 (15.1)	0	0	0
Anaemia	8 (15.1)	0	0	0
Alanine aminotransferase increased	7 (13.2)	0	0	0
Gamma-glutamyltransferase increased	6 (11.3)	0	0	0
Blood thyroid stimulating hormone increased	6 (11.3)	0	0	0
Hypothyroidism	6 (11.3)	0	0	0
Blood creatine phosphokinase increased	6 (11.3)	0	0	0
Hyperuricaemia	6 (11.3)	0	0	0

1. Partnered with Biotheus Inc.:

irAEs = immune related adverse events; (n)ccRCC = (non-)clear cell renal cell carcinoma; SAEs = serious adverse events; TRAEs = treatment related adverse events;

BNT327/PM8002¹ (RCC) – ESMO 2024 Data: Key Takeaway Messages



Efficacy:

BNT327/PM8002¹ showed encouraging anti-tumor activity:

ccRCC Cohort (n = 28 evaluable patients)

- ORR was 25.0% with 7 confirmed PR, 16 SD, and 5 PD, DCR was 82.1%
- mPFS was 10.9 months (95% CI: 5.7, NE), mDoR 19.6 months (95% CI: 4.2, NE)

nccRCC Cohort (n = 22 evaluable patients)

- ORR was 36.4% with 8 PR (7 confirmed) and 12 SD, DCR was 90.9%.
- mPFS was 15.1 months (95% CI: 5.7, NE).
- Responses were observed across subtypes of nccRCC. The highest ORR (60%) was among patients with papillary.



Safety Profile:

BNT327/PM8002¹ showed manageable safety in patients with previously untreated advanced nccRCC or advanced ccRCC after failure of the combination of anti-PD-1/L1 and VEGF-TKI therapy or VEGF-TKI monotherapy.



Outlook:

Further clinical development in RCC is warranted.

1. Partnered with Biotheus Inc.;
CI = confidence interval; DCR = disease control rate; DOR = duration of response; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; (n)ccRCC = (non-)clear cell renal cell carcinoma; NE = not evaluable; ORR = overall response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; VEGF TKI = Vascular endothelial growth factor tyrosine kinase inhibitors.

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BNT316 / ONC-392¹

Platinum-Resistant Ovarian Cancer

PRESERVE-004/GOG-3081 (NCT05446298):

A Phase 2 randomized dose optimization trial of gotistobart, a pH-sensitive anti-CTLA-4, in combination with pembrolizumab in platinum-resistant ovarian cancer

Joyce N. Barlin (Women's Cancer Care Associates, Albany, NY, United States) et al., Presentation Number: LBA32

1. Partnered with OncoC4

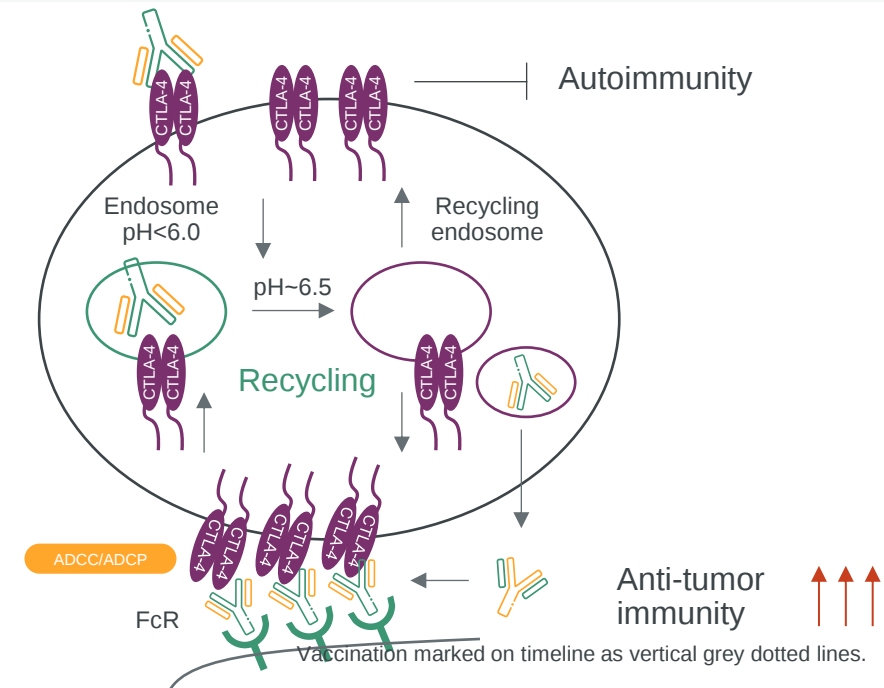
BIONTECH

BNT316/ONC-392 (Gotistobart)¹ is a pH-sensitive CTLA-4-preserving Antibody with the Potential to Become Best-in-Class

Avoiding lysosomal degradation of CTLA-4 for safer and more effective immunotherapy may lead to uncoupling cancer therapeutic effect from immunotherapy-related adverse effects

BNT316/ONC-392 (gotistobart)¹ designed to:

- Allow regular recycling and enrichment of antibody and CTLA-4 molecule
- Enhance anti-tumor immunity
- Reduce immune-related adverse events



MoA designed to allow higher dosing & longer duration of treatment with BNT316/ONC-392 (gotistobart)¹

Liu Y. et al. Abstract # 231, SITC 2021. Du et al. Uncoupling therapeutic from immunotherapy-related adverse effects for safer and effective anti-CTLA-4 antibodies in CTLA4 humanized mice. Cell Res. 2018 Apr; 28(4): 416–432. Du et al. A reappraisal of CTLA-4 checkpoint blockade in cancer immunotherapy. Cell Res. 2018 Apr; 28(4): 433–447.

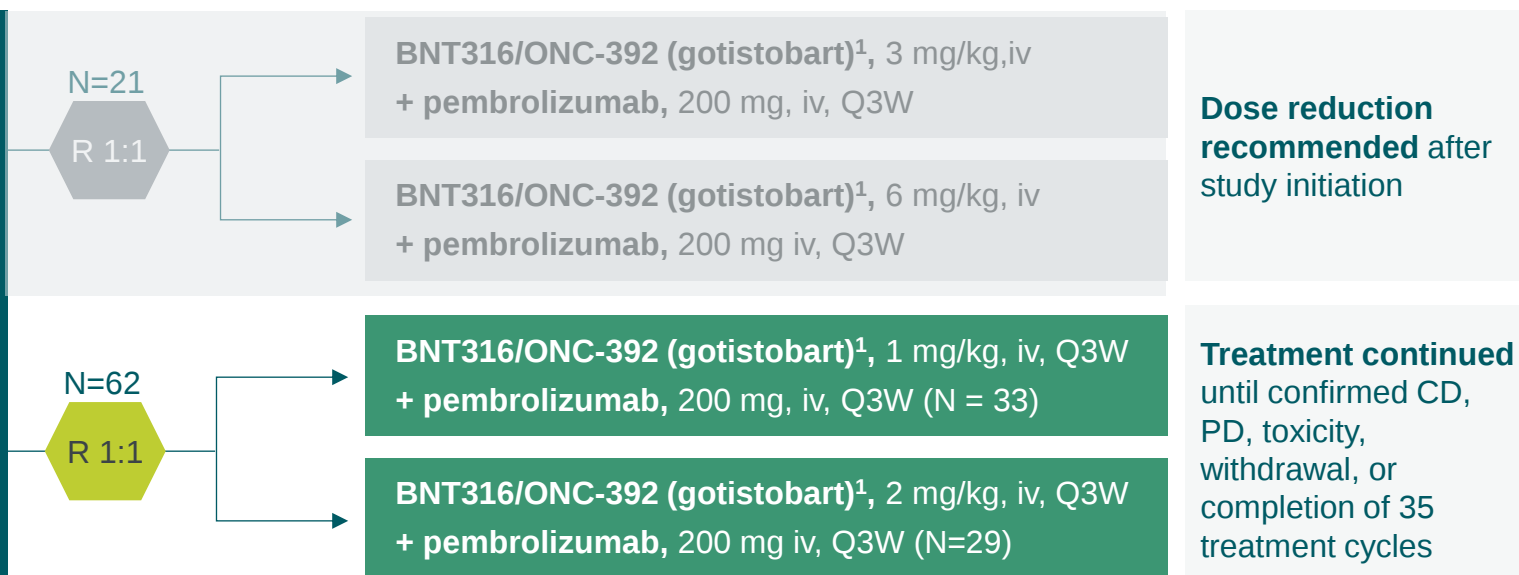
1. Partnered with OncoC4. ADCC = antibody-dependent cell-mediated cytotoxicity, ADCP = antibody-dependent cellular phagocytosis; CTLA-4 = cytotoxic T-lymphocyte-associated protein 4, FcR = fragment crystallizable region.

BNT316/ONC-392 (Gotistobart)¹ in Combination with Pembrolizumab in Patients with Platinum-Resistant Ovarian Cancer (PRESERVE-004)

Phase 2 randomized, open-label, multicenter study to evaluate safety and efficacy of BNT316/ONC-392 (gotistobart)¹ in combination with pembrolizumab in patients with PROC ([NCT05446298](#))

Inclusion criteria

- Age ≥ 18 years
- Prior SoC of surgical intervention, including hysterectomy and salpingo-oophorectomy
- Resistant to platinum-based CTx and disease progression on therapy containing bevacizumab
- More than 1 prior systemic lines of anti-cancer therapy
- Measurable lesions (RECIST 1.1)
- ECOG score 0-1



Key endpoints

Primary:

Secondary:

Exploratory:

ORR (by INV per RECIST 1.1), irAEs, TRAEs, TRSAEs

DoR, DCR, BoR, PFS, OS

PK, ER, TRAE-related study discontinuation

1. Partnered with OncoC4

BOR = best overall response; CTx = chemotherapy; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; irAEs = immune-related adverse events; ORR = objective response rate; OS = overall survival; PK/PD = pharmacokinetics/pharmacodynamics; PARP = poly (ADP-ribose) polymerase; PFS = progression-free survival; PROC = platinum-resistant ovarian cancer; Q3W = every three weeks; RECIST = Response Evaluation Criteria in Solid Tumors; SoC = standard of care; TRAEs = treatment-related adverse events.

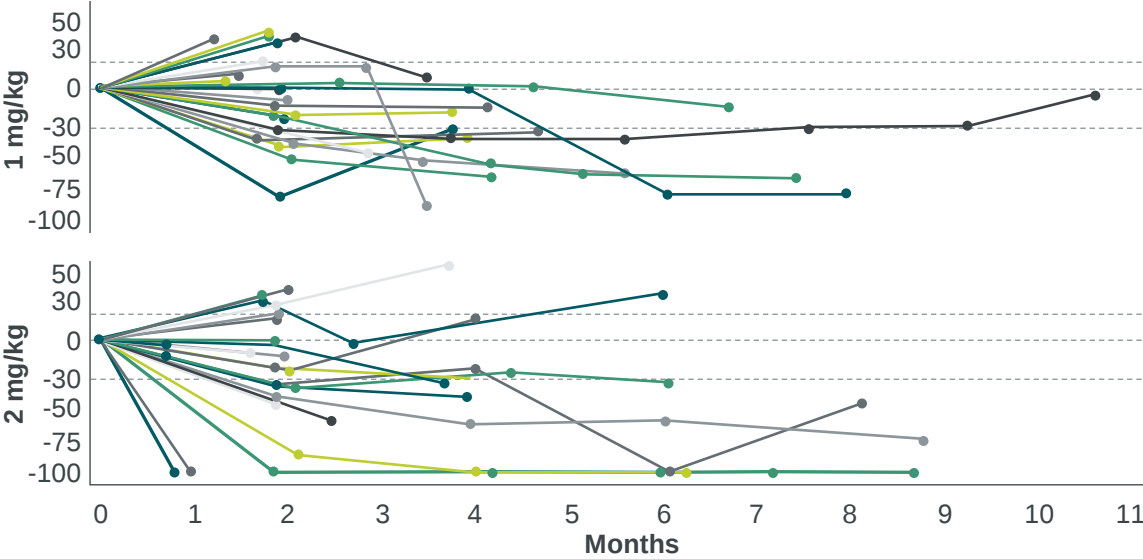
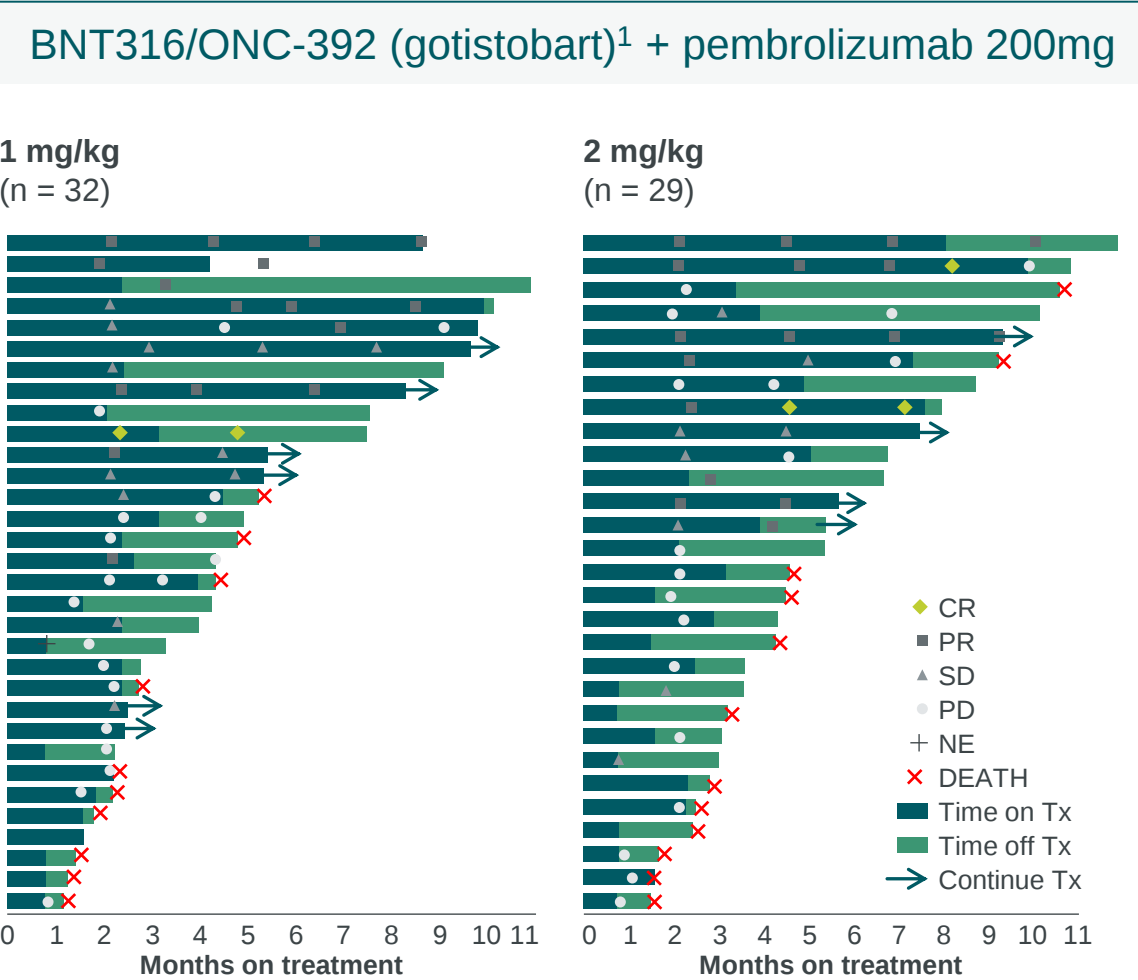
PRESERVE-004: Baseline Disease Characteristics and Study Drug Exposure

Characteristic	BNT316/ONC-392 (gotistobart) ¹ + pembrolizumab 200mg	
	1 mg/kg (n = 33)	2 mg/kg (n = 29)
Age – median (range), years	65.2 (10.25)	63.5 (8.46)
Race – n (%)		
White/ Black/ Asian/ Other	27 (81.8)/ 1 (3.0)/ 1 (3.0)/ 3 (9.1)	25 (86.2)/ 2 (6.9)/ 1 (3.4)/ 1 (3.4)
ECOG performance-status score – n (%)		
0	19 (57.6)	15 (51.7)
1	14 (42.4)	14 (48.3)
Primary cancer diagnosis n (%)		
High-grade serous ovarian cancer	28 (84.8)	25 (86.2)
Primary peritoneal cancer	3 (9.1)	2 (6.9)
Fallopian tube cancer	2 (6.1)	2 (6.9)
Metastatic disease at enrolment, n (%)	24 (72.7)	25 (86.2)
Prior cancer regimens – median (range)	4.0 (2–9)	3.0 (1–8)
BEV-naïve, n (%)	6 (18.2)	12 (41.4)
Study drug exposure		
Treatment duration, mean months (SD)	3.03 (2.43)	3.18 (2.45)
Gotistobart cycles, median (range)	3.0 (1–12)	3.0 (1–12)
Gotistobart dose intensity, % (range)	98.4 (56.6–106.9)	98.4 (56.7–105.1)

Data cut-off: July 19, 2024.

1. Partnered with OncoC4;
BEV = Bevacizumab; ECOG = Eastern Cooperative Oncology Group; SD = standard deviation.

BNT316/ONC-392 (Gotistobart)¹ Plus Pembrolizumab Showed Encouraging Preliminary Efficacy



	BNT316/ONC-392 (gotistobart) ¹ + pembrolizumab 200mg	
	1 mg/kg (N=32)	2 mg/kg (N=29)
ORR (unconfirmed) % (n)	25.0% (8)	27.6% (8)
95% CI	11.5 – 43.4	12.7 – 47.2
Complete response ^{a,b}	3.1% (1)	6.9% (2)
Partial response ^a	21.9% (7)	20.7% (6)
Stable disease	21.9% (7)	13.8% (4)
Progressive disease	40.6% (13)	44.8% (13)
No post-baseline assessment ^c	12.5% (4)	13.8% (4)

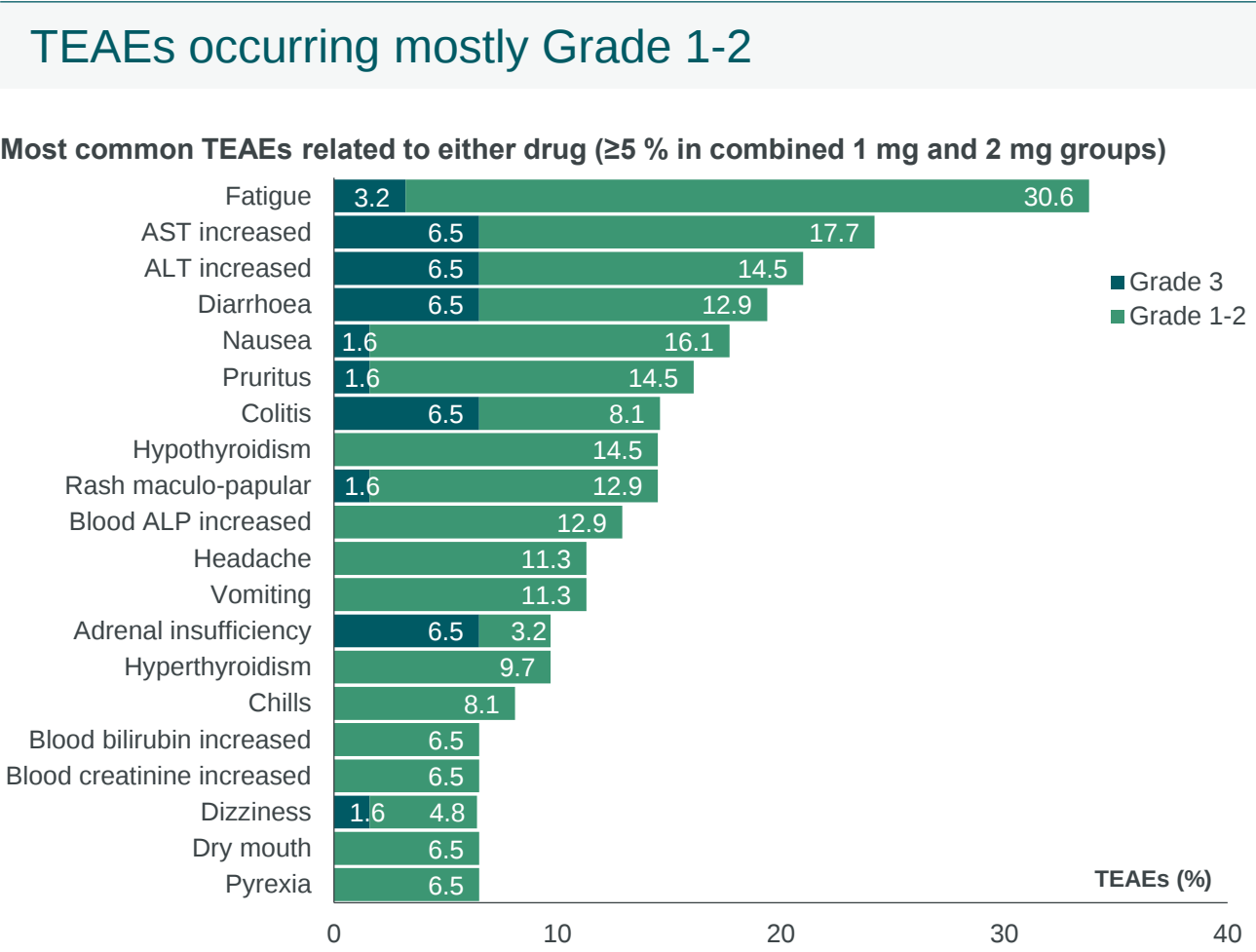
Data cut-off: July 19, 2024.

1.Partnered with OncoC4; a. Includes both confirmed and unconfirmed responses (3 unconfirmed responders in each treatment group); b. One out of 3 unconfirmed responders are still on treatment, for both treatment groups; c. Patients died or discontinued from study without any post-baseline scan. CR = complete response; ORR = objective response rate; PD = progressive disease; PR = partial response; SD = stable disease.

BNT316/ONC-392 (Gotistobart)¹ Showed Manageable Tolerability Profile at Both Dose Levels

Safety summary		
Gotistobart ¹ + pembrolizumab 200 mg		
	1 mg/kg N = 33	2 mg/kg N = 29
TEAEs, n (%)	33 (100.0)	28 (96.6)
Grade ≥ 3, n (%)	25 (75.8)	25 (86.2)
TEAEs related to either drug, n (%)	27 (81.8)	23 (79.3)
Grade ≥ 3, n (%)	15 (45.5)	12 (41.4)
Serious TEAEs	18 (54.5)	21 (72.4)
irAE All grades, n (%)	15 (45.5)	18 (62.1)
Grade ≥ 3, n (%)	8 (24.2)	11 (37.9)
TEAEs leading to gotistobart discontinuation	7 (21.2)	8 (27.6)

Data cut-off: July 19, 2024.



1.Partnered with OncoC4;
ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate aminotransferase; irAE = immune-related adverse event; SD = standard deviation ; TEAE = treatment emergent adverse event.

Gotistobart¹ – ESMO 2024 Data: Key Takeaway Messages



Efficacy

Preliminary results for efficacy are encouraging

The final dose selection will be based on the totality of safety, efficacy, and pharmacology



Safety Profile

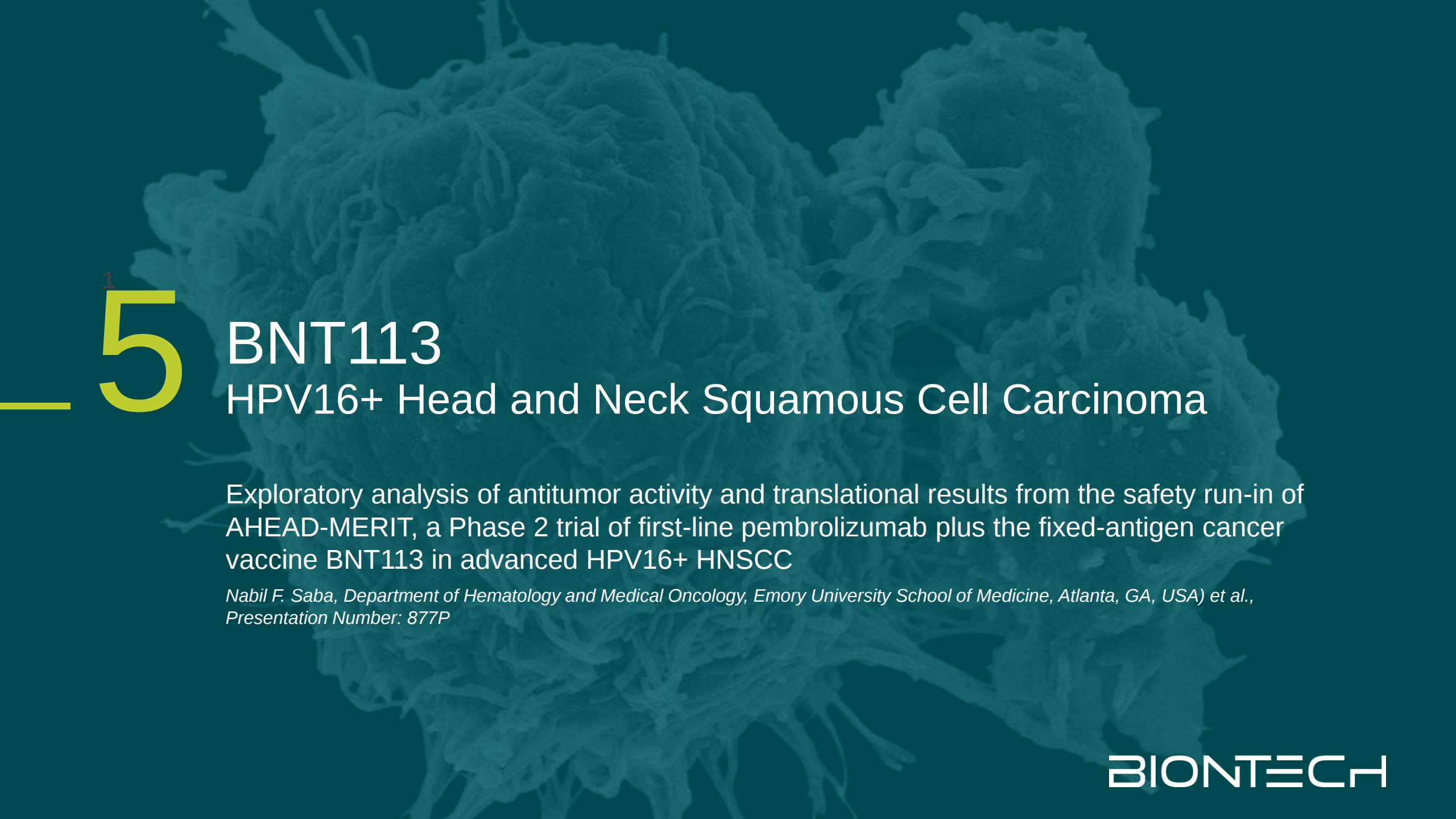
Early results from PRESERVE-004 demonstrate that gotistobart + pembrolizumab in PROC has a manageable tolerability profile at both dose levels, with no new safety signals



Outlook

If confirmed by further preplanned analyses, the combination of gotistobart plus pembrolizumab in PROC may be explored in a randomized setting

1.Partnered with OncoC4;
PROC = platinum-resistant ovarian cancer



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BNT113

HPV16+ Head and Neck Squamous Cell Carcinoma

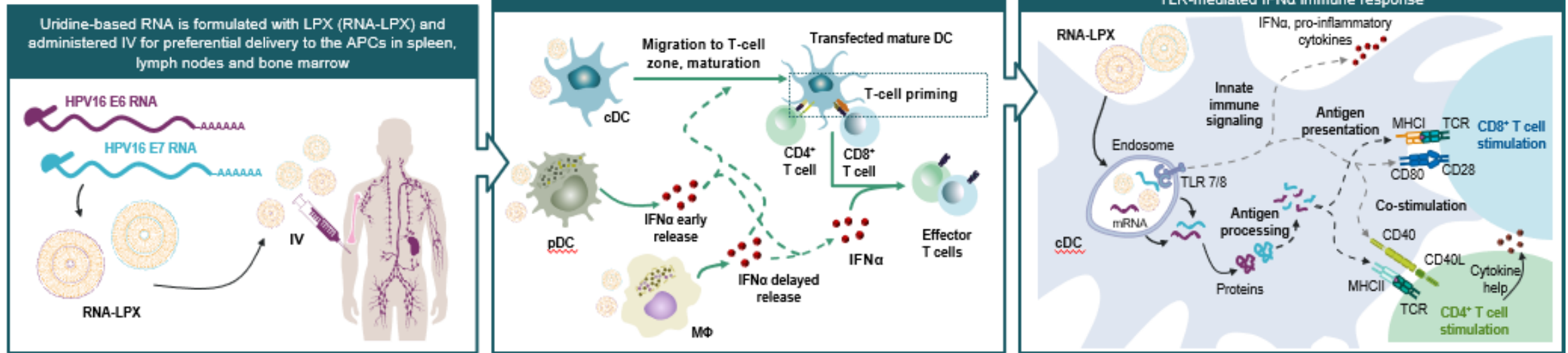
Exploratory analysis of antitumor activity and translational results from the safety run-in of AHEAD-MERIT, a Phase 2 trial of first-line pembrolizumab plus the fixed-antigen cancer vaccine BNT113 in advanced HPV16+ HNSCC

*Nabil F. Saba, Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA, USA) et al.,
Presentation Number: 877P*

BIONTECH

BNT113 FixVac Proposed Mechanism of Action

Figure 1. Proposed mechanism of action of FixVac



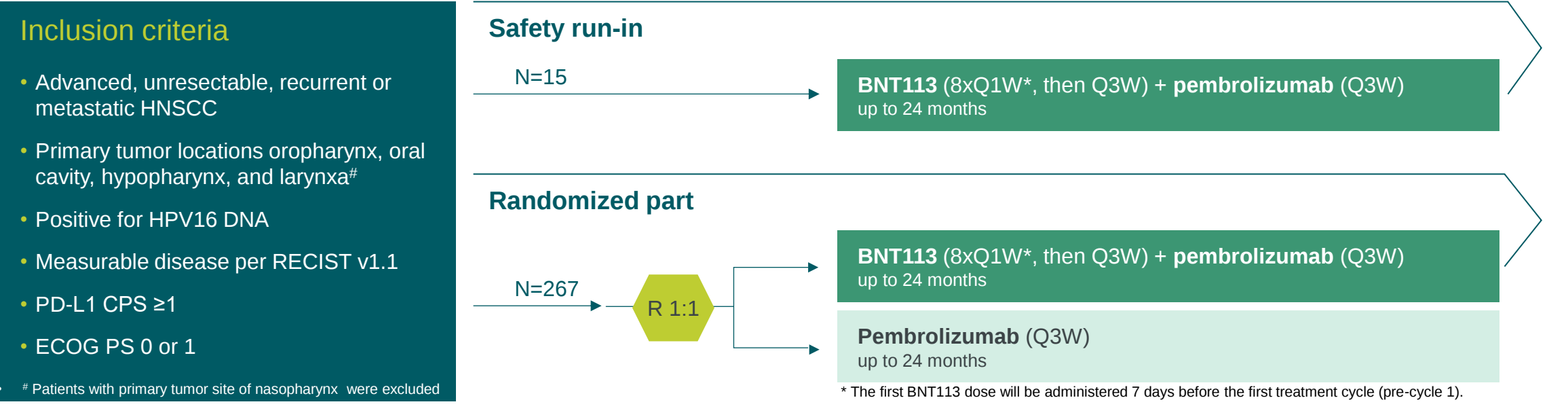
Background information:

- BNT113 is an investigational uridine-based mRNA-lipoplex (LPX) cancer immunotherapy encoding the human papillomavirus (HPV)16 oncoproteins E6 and E7^{1,2}
- Intravenously administered RNA-LPX is preferentially delivered to dendritic cells (DCs), leading to DC maturation, activation of type I interferon (IFN)-driven immunity, and induction of profound antigen-specific T-cell responses (Figure 1)³
- The preliminary analysis of the safety run-in of AHEAD-MERIT suggested that BNT113 in combination with pembrolizumab was well tolerated; the safety profile was consistent with that expected for this combination⁴

1. Pinatti LM, et al. J Dent Res. 2018; 97(6): 691–700; 2. Tran NH, et al. J Med Virol. 2024;96:e29746; 3. Kranz L, et al. Nature 2016;534:396–401; 4. Klinghammer K, et al. IOTECH 2022;16(suppl_1):19; doi: 10.1016/j.iotech.2022.100267.
APC = antigen-presenting cell; cDC = classical dendritic cell; DC = dendritic cell; HPV = human papillomavirus; IFN = interferon; IV = intravenous; LPX = lipoplex; NF-κB = nuclear factor kappa B; MΦ = macrophage; MHC = major histocompatibility complex; pDC = plasmacytoid dendritic cell; TCR = T-cell receptor; TLR = toll-like receptor.

BNT113 in Combination with Pembrolizumab as 1L Treatment in Patients with R/R HPV16+ HNSCC Expressing PD-L1 (AHEAD-MERIT)

Phase 2 open-label, controlled study to confirm safety and efficacy of BNT113 in combination with pembrolizumab as 1L treatment in patients with metastatic HNSCC ([NCT04534205](#))



	Endpoints	Safety run-in	Randomized part
	Primary:	TEAEs; <i>up to 27 months</i>	OS, ORR; <i>up to 48 months</i>
	Secondary:	ORR, DoR, DCR	INV-ORR, PFS, DCR, DOR, safety
	Exploratory:	PFS, OS, biomarkers	

1L = first line; CPS = combined positive score; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; INV = investigator assessed; iv = intravenously; HNSCC = head and neck squamous cell carcinoma; HPV16 = human papilloma virus 16; ORR = objective response rate; OS = overall survival; PD-L1 = programmed cell death protein ligand 1; PFS = progression free survival; Q3W = every three weeks; RECIST = Response Evaluation Criteria in Solid Tumors; R/M = recurrent/metastatic; R/R = relapsed/refractory; TEAE = treatment emergent adverse event.

BNT113 AHEAD-MERIT Trial Baseline Patient and Disease Characteristics – All Patients

Study status

As of 24 June 2024, **N=15 patients were enrolled** in the safety run-in part and received BNT113+pembrolizumab

Median exposure to BNT113 was 7.0 months (range, 1.6–24.4 months)



Characteristic	N=15
Age, median (range), years	66.0 (41–74)
Male, n (%)	15 (100)
ECOG PS=0, n (%)	10 (66.7)
ECOG PS=1, n (%)	5 (33.3)
Disease status, n (%)	
Metastatic disease	6 (40.0)
Unresectable recurrent	6 (40.0)
Metastatic and unresectable recurrent	2 (13.3)
Missing	1 (6.7)
PD-L1 CPS, n (%)	
CPS ≥20	7 (46.7)
CPS 1–<20	7 (46.7)
CPS <1 ^a	1 (6.7)
Primary location, n (%)	
Hypopharynx	1 (6.7)
Larynx	0
Oral cavity	1 (6.7)
Oropharynx	13 (86.7)
Prior platinum (early setting)	11 (73.3)

Data cut-off: June 24, 2024.

a. Patient 104 was enrolled based on positive CPS. CPS = combined positive score; ECOG PS = Eastern Cooperative Oncology Group performance status; PD-L1 = programmed cell death ligand 1;

BNT113 in Combination with Pembrolizumab was Well Tolerated

Safety observations

The safety analysis set included all 15 patients

The most frequently occurring TEAEs were pyrexia, chills, fatigue, nausea, influenza-like illness and hypothyroidism

There was one fatal TEAE of pulmonary sepsis (considered not related to study treatment)

Grade 3–4 TEAEs were reported in 7 patients (46.7%) and were considered related in 2 patients (13.3%):

- n=1 patient reported Grade 3 pyrexia and Grade 3 anemia; n=1 patient reported Grade 3 decreased appetite

Analysis of the safety run-in cohort of AHEAD-MERIT confirmed TEAEs were mostly Grade 1–2

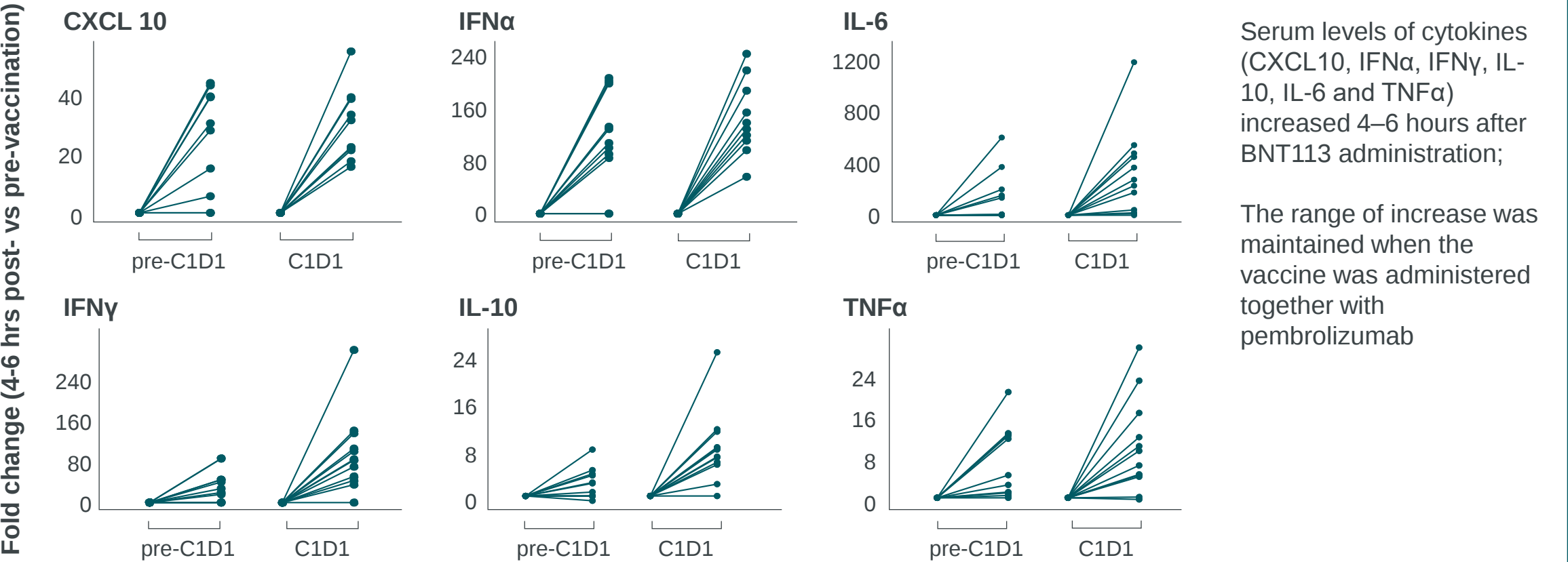
Patients reporting TEAE, n (%)	N=15 ^a		TEAEs reported in >1 patient ^c	Grade 1–2	Grade 3–4
	All grades	Grade ≥3			
Any TEAE	15 (100)	8 (53.3)	Pyrexia	9 (60.0)	1 (6.7)
Number of events	309	18	Chills	9 (60.0)	-
Any related TEAE	15 (100)	2 (13.3)	Fatigue	8 (53.3)	1 (6.7)
Any TESAE		7 (46.7)	Nausea	5 (33.3)	-
TESAE related to:			Hypothyroidism	4 (26.7)	-
BNT113		2 (13.3)	Influenza-like illness	4 (26.7)	-
Pembrolizumab		3 (20.0)	Anemia	1 (6.7)	2 (13.3)
Any TESAE leading to death		1 (6.7) ^b	Decreased appetite	2 (13.3)	1 (6.7)
Any TEAE leading to discontinuation of:			Constipation	3 (20.0)	-
BNT113	0		Vomiting	3 (20.0)	-
Pembrolizumab	1 (6.7)		Abdominal pain (upper)	1 (6.7)	1 (6.7)
			Hypercalcemia	1 (6.7)	1 (6.7)
			Back pain	2 (13.3)	-
			Dermatitis acneiform	2 (13.3)	-
			Dyspepsia	2 (13.3)	-
			Headache	2 (13.3)	-
			Hypertension	2 (13.3)	-
			Tachycardia	2 (13.3)	-

a. Analysis includes patient 104, who was enrolled based on local positive CPS; b. Pulmonary sepsis (n=1); c. The table shows TEAEs of any grade that were reported in >1 patient. The following TEAEs were reported in n=1 patient each as Grade 3–4: acute pancreatitis, cholangitis, cholangitis sclerosing, cholecystitis, circulatory collapse, decreased weight, duodenitis, gastritis, pleural effusion, pneumonia aspiration. TEAE= treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.

Data cut-off: June 24, 2024.

BNT113 Triggered an Immune Response, Evidenced by Post-Vaccination Increase of Serum Levels of CXCL10, IFN α , IFN γ , IL-10, IL-6 and TNF α

Change in serum cytokine level – safety analysis set

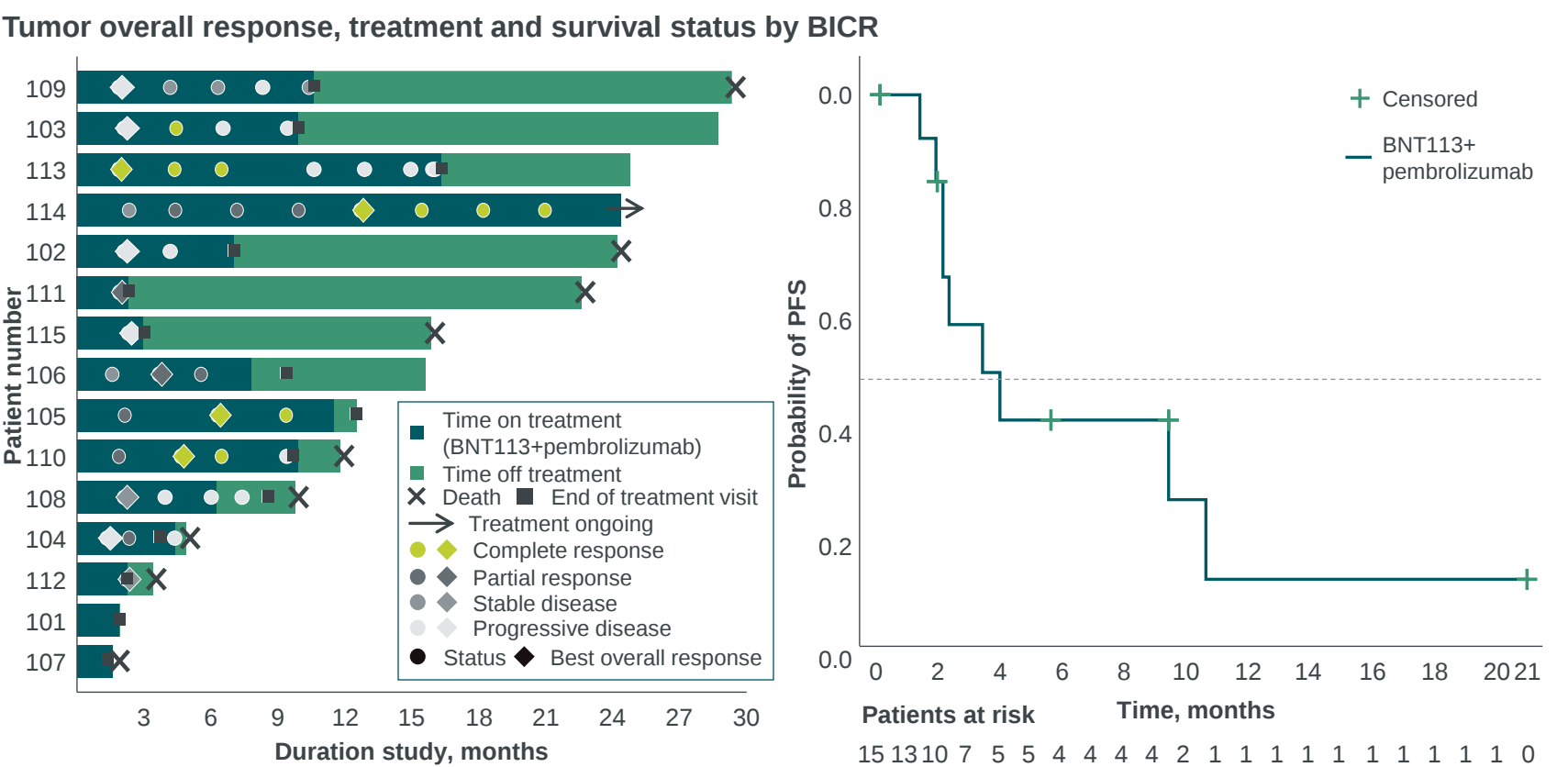


Individual patient data are shown as fold change in cytokine levels 4–6 hours post-versus pre-vaccination at pre-C1D1 (first BNT113 administration) and at C1D1 (BNT113 plus pembrolizumab administration). Data were normalized to baseline; values below LLOQ were set to LLOQ/2. C1D1 = cycle 1 day 1; CXCL = chemokine (C-X-C motif) ligand; IFN = interferon; IL = interleukin; LLOQ = lower limit of quantification; TNF = tumor necrosis factor..

BNT113 Showed Encouraging Efficacy with Unconfirmed ORR (BICR) of 40%

The efficacy analysis set was defined as all patients who received at least one dose of BNT113 (N=15)
Patient 104, who was enrolled based on local positive CPS result, was included in this analysis.

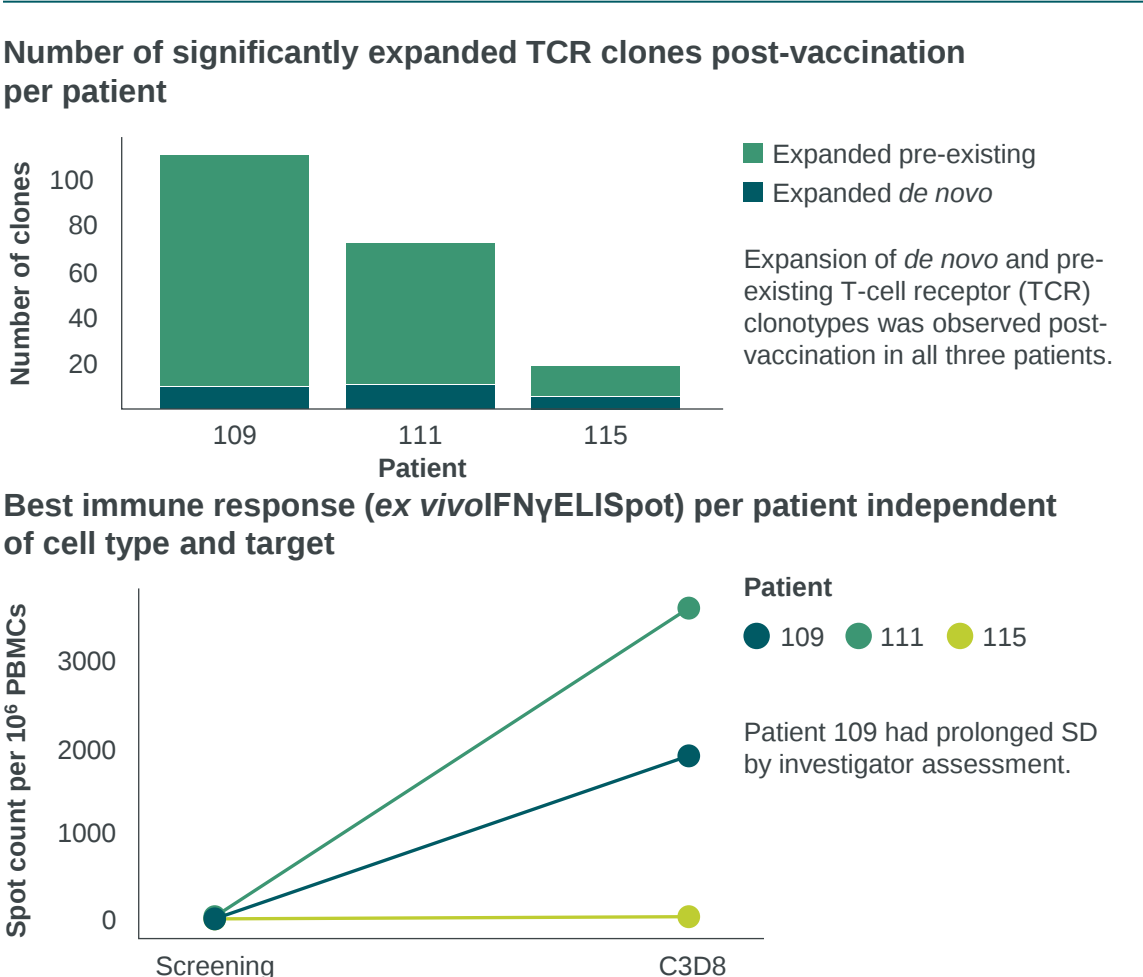
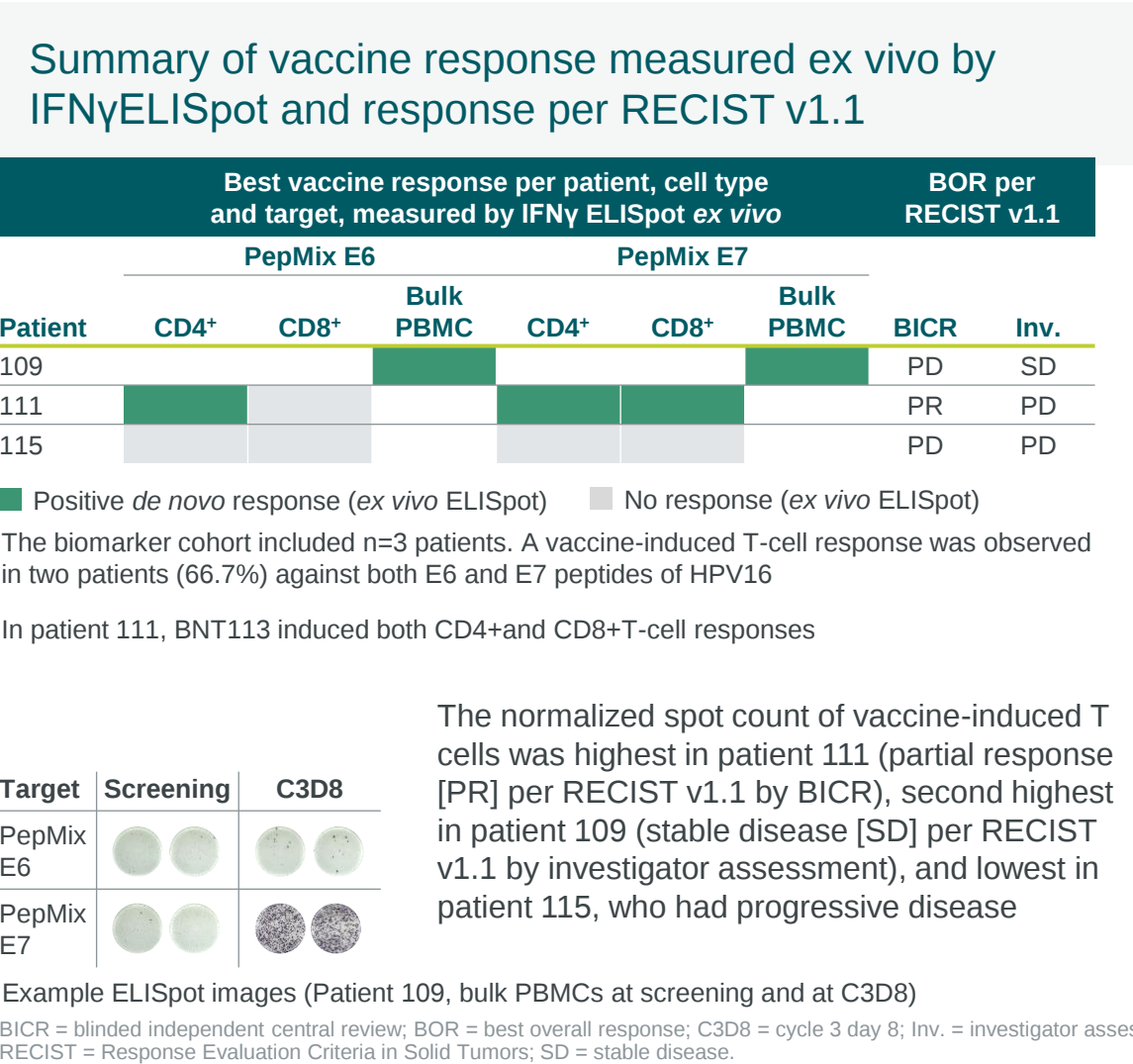
Antitumor activity	N=15
Unconfirmed ORR (BICR), %	40.0
CR, n	4
PR, n	2
Unconfirmed DCR (BICR), %	53.3
Unconfirmed ORR (investigator), %	33.3
Unconfirmed DCR (investigator), %	60.0
PFS by BICR	
Median (95% CI), months	3.9 (2.1–10.6)
6-month rate, %	42.3
12-month rate, %	14.1
18-month rate, %	14.1
PFS by investigator	
Median (95% CI), months	6.0 (2.3–10.4)
OS, median (95% CI), months	22.6 (9.8–NE)



Data cut-off: 24 June 2024

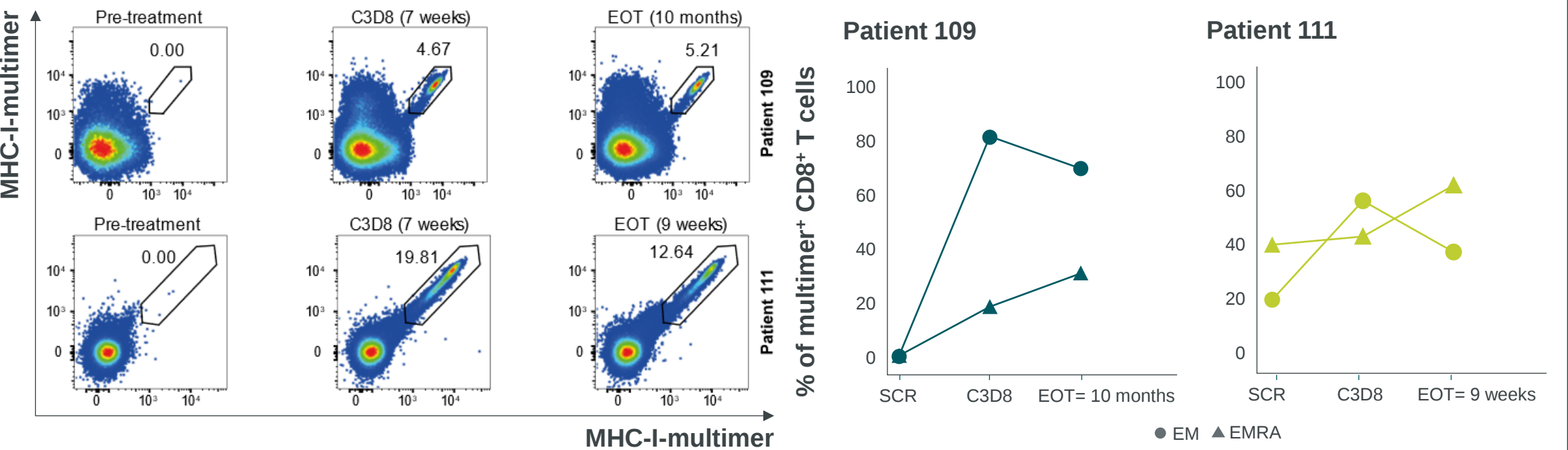
BICR = blinded independent central review; CI = confidence interval; CR = complete response; DCR = disease control rate; NE = not estimable; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response.

BNT113-Induced T-cell Response and Clonotype Expansion Post-Vaccination in Biomarker Cohort (n=3)



Large Portion of BNT113 Induced Antigen-Specific Peripheral T Cells had an Effector Memory Phenotype

Detection and phenotyping of vaccine antigen-specific peripheral T cells (n=2)



MHC-I-multimer staining of PBMCs revealed that, in two patients, **vaccine (E7) antigen-specific CD8⁺T cells** that appeared de novo by C3D8 **were detectable until the end of treatment** (10 months for patient 109 and 9 weeks for patient 111)

A large proportion of **vaccine antigen-specific multimer⁺CD8⁺T cells displayed an effector memory (EM) phenotype** with increasing CD45RA and CD57 positivity over time.

BNT113 (HPV16+ HNSCC) – ESMO 2024 Data: Key Takeaway Messages



Safety Profile:

Analysis of the safety run-in cohort confirmed combination of BNT113 and pembrolizumab was well tolerated: TEAEs were mostly Grade 1–2



Efficacy:

Data from the biomarker cohort (n=3) showed that BNT113 induced *de novo* T-cell responses against HPV16 E6 and E7 antigens

- All three patients had an expansion of pre-existing or *de novo* TCR clonotypes post-vaccination; expansion was more pronounced in two patients who had T-cell response on *ex vivo* ELISpot
- In two patients with T-cell responses on *ex vivo* ELISpot, vaccine antigen-specific CD8+T cells were detectable in peripheral blood until the end of treatment
- A large proportion of vaccine antigen-specific peripheral T cells had an effector memory phenotype

ORR was 40.0% (BICR) and 33.3% (investigator), and median PFS was 3.9 months (BICR) and 6.0 months (investigator)

In the exploratory cohort, BNT113 triggered an immune response, as evidenced by a post-vaccination increase of serum levels of CXCL10, IFN α , IFN γ , IL-10, IL-6 and TNF α



Outlook:

The randomized part of the study is ongoing; patient recruitment is open in Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Czech Republic, France, Germany, Hungary, Italy, Mexico, Poland, Portugal, Republic of Korea, Spain, Sweden, Taiwan, Turkey, the United Kingdom and the United States

BICR = blinded independent central review; CD = cluster of differentiation; CXCL = chemokine; HNSCC = head and neck squamous cell carcinoma; HPV16 = human papilloma virus 16; IFN = interferon; IL = interleukin; ORR = objective response rate; PFS = progression-free survival; TCR = T-cell response; TNF = tumor necrosis factor.

¹
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BNT113 – HARE-40 (IIT) HPV16+ Carcinomas

HARE-40: A phase I/II trial of therapeutic HPV vaccine (BNT113) in patients with HPV16 driven carcinoma

Christian H. Ottensmeier, MD, PhD, FRCP (Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, University of Liverpool, University of Southampton, UK) et al.; Presentation Number: 27LO

BIONTECH

BNT113 (FixVac) as HPV Anti-CD40 RNA Vaccine Monotherapy in Patients with HPV16+ Head and Neck Cancer and other HPV16+ Cancers (HARE-40) (IIT)

An Investigator-Initiated Phase 1/2 vaccine dose escalation study to evaluate safety, tolerability and recommended dose of BNT113 as monotherapy in patients with HPV16+ cancers ([NCT03418480](#))

Arm 1A (n=17):

- HPV16+ HNSCC adjuvant

Cohort 1

BNT113, iv, Q1W x 4 then Q2W x 4
Intra-patient dose escalation from 7.2 µg to 29 µg

Cohort 2

BNT113, iv, Q1W x 4 then Q2W x 4
Intra-patient dose escalation from 7.2 µg to 72.8 µg

Arm 1B (n=13)*:

- HPV16+ advanced cancers, no SOC options
 - anal cancer (n=5)
 - HNSCC (n=3)
 - cervical (n=2)
 - other cancers (n=3)

*1 patient received DTH assessment but did not receive drug

BNT113, iv, Q1W x 4 then Q2W x 4
Intra-patient dose escalation from 7.2 µg to 72.8 µg

If clinically indicated,
treatment
beyond dose 8
and
up to 1 year
allowed.

CD = cluster of differentiation; DTH = delayed type hypersensitivity; HNSCC = head and neck squamous cell carcinoma; HPV16+ = human papilloma virus 16-positive; IIT=investigator initiated trial; QxW = every x week; SOC = standard of care.

BNT113 was Overall Well Tolerated with Manageable Safety Profile

Common AEs (≥20%), n (%)	N=30	Event grade ≥3
Nausea	13 (43%)	0
Fatigue	13 (43%)	1
Headache	12 (40%)	0
Chills	7 (23%)	0
Constipation	6 (20%)	1
Back pain	6 (20%)	0
Cough	6 (20%)	0

- N=30 patients were included in the safety analysis
- 19/30 (63%) patients received 8 doses of BNT113
- 2 patients in Arm 1A met individual MTD^a
- No SAE with fatal outcome

^a These patients did not experience a DLT but met their individual MTD as defined by the Safety Review Committee.

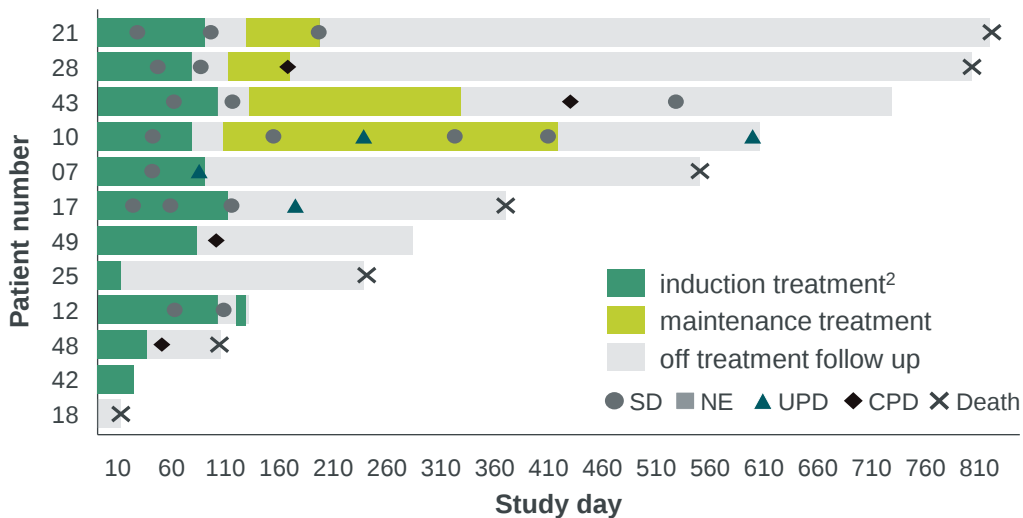
Reason for treatment discontinuation, n (%)	N=30
Subject withdrawal	5 (17%)
Disease progression	2 (7%)
Unacceptable toxicity	1 (3%)
Other/missing	3 (10%)

Related AEs, n (%)	Grade	N=30
Within 1 week	≥1	26 (87%)
Within 90 days	≥3	7 (23%)
(Pre)-Syncope		4 (one patient)
Fatigue		1
IRR ^b		1
Hypotension		2

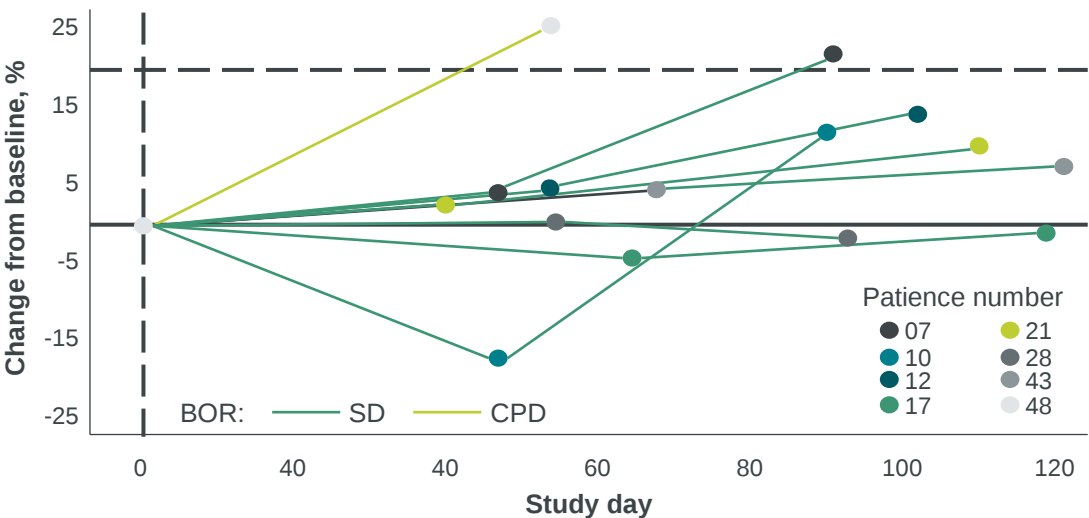
^b Includes patients reporting preferred term IRR per CTCAE Version 4.03.

BNT113: Preliminary Efficacy Assessment

Time of treatment, disease response¹, and follow-up in arm 1B



Change of irRECIST target lesion from baseline until EoT – arm 1B



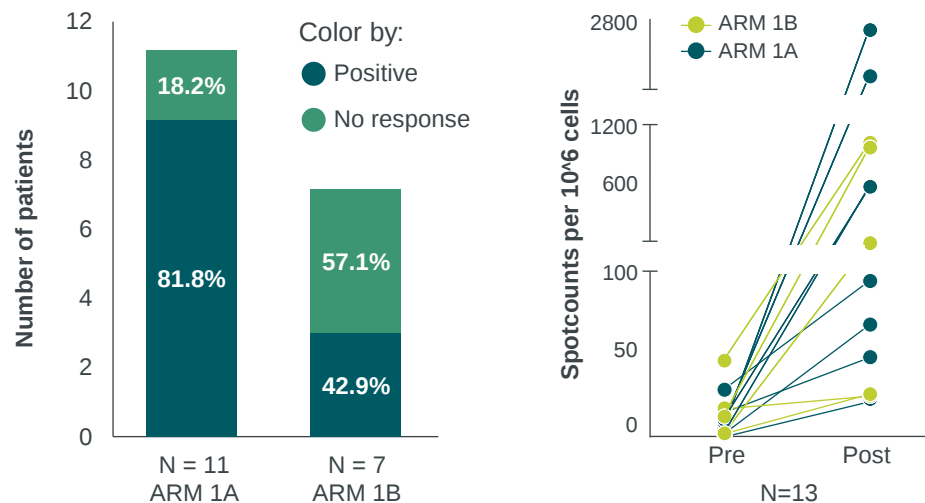
- Median follow up in Arm 1B: 26.5 months
- DCR at EoT: 71% (95% CI: 29-96%, 7 evaluable patients)
- 5 patients received maintenance treatment in Arm 1B

Disease response ¹ at EoT, n (%)	N=9
Stable disease	5 (71%)
Unconfirmed progression	1 (14%)
Confirmed progression	1 (14%)
Not evaluable	1
Missing eCRF	1

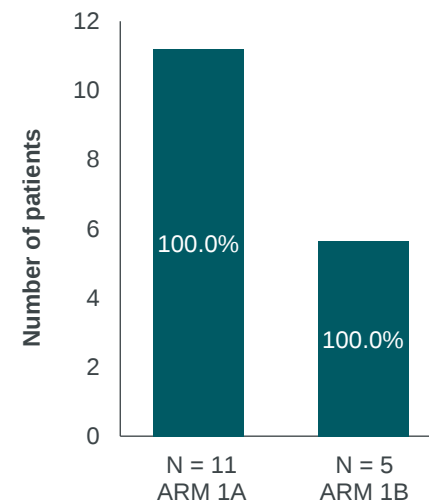
¹ Responses evaluated per irRECIST. ² Time until end of induction treatment visit is depicted. BOR = best overall response; CI = confidence interval; CPD = confirmed progression; DCR = disease control rate; eCRF = electronic case report form; EoT = end of treatment; irRECIST = Immune-related Response Evaluation Criteria In Solid Tumors; NE = not evaluable; SD = stable disease; UPD = unconfirmed progression.

BNT113 Showed Robust Immune Responses in Adjuvant and Advanced Disease

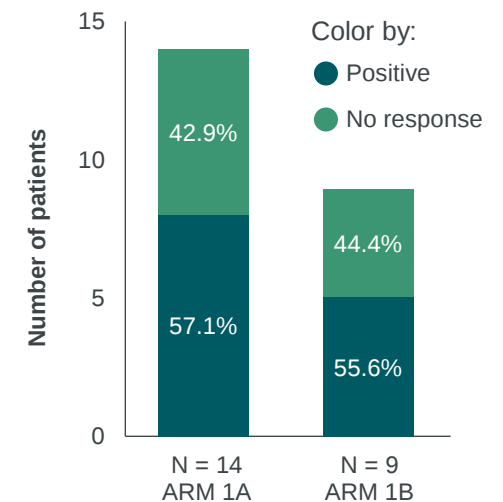
ex vivo IFN γ ELISpot responses to E6 and/or E7 peptide pools



ivS IFN γ ELISpot responses to E6/E7 peptide pools



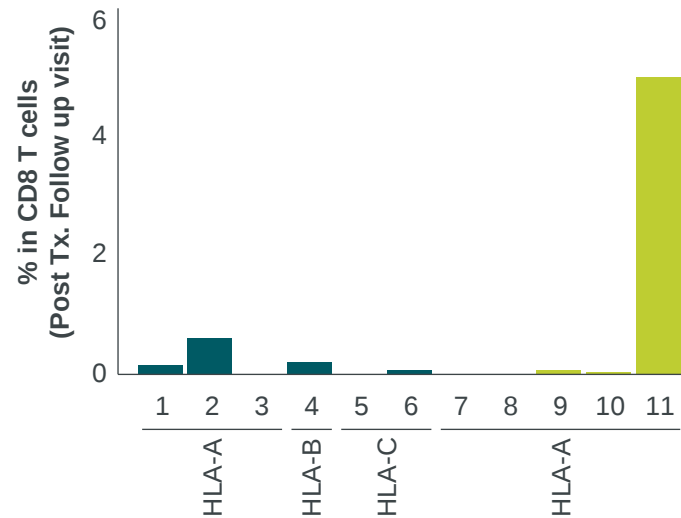
Anti-E7 IgG antibody responses (ELISA)



- 66.7% (12/18 evaluable patients): vaccine-induced E6/E7 responses by ex-vivo ELISpot. 9/11 in Arm 1A; 3/7 in Arm 1B
- 100% (16/16 evaluable patients): IFN γ E6/E7 response by post *ivS* ELISpot assay
- Anti E7 IgG antibody response in ~56% of patients in both arms

BNT113 Vaccine-Induced T cell Tracking and Phenotypic Characterization

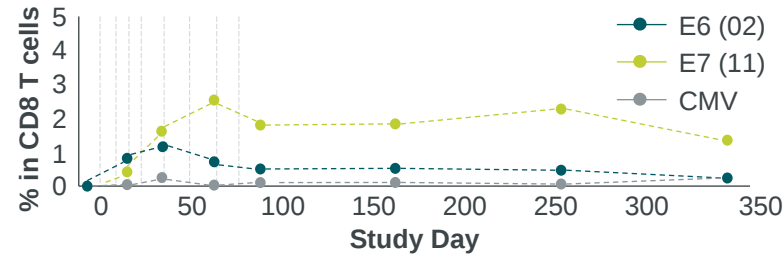
Individual patient multimer screening



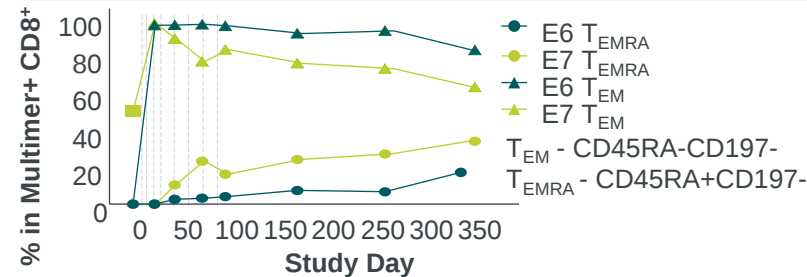
Individual patient with vaccine response:
Patient 08
Arm 1A Cohort 2
Adjuvant setting 72.8 µg dose reached

■ E6 Multimers
■ ET Multimers
■ CMV

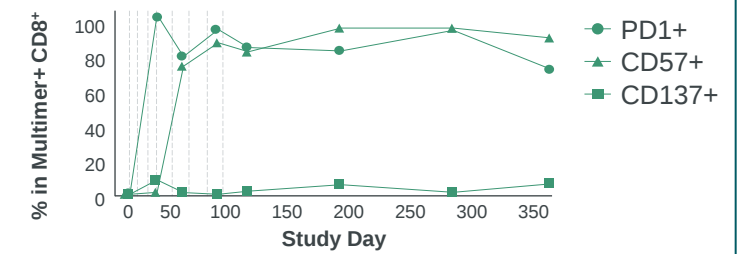
Kinetic assessment of multimer⁺CD8⁺ T cells



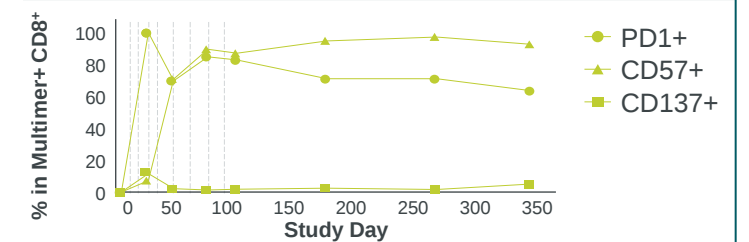
Phenotype of multimer⁺CD8⁺ T cells



Phenotype of E6 multimer⁺CD8⁺ T cells



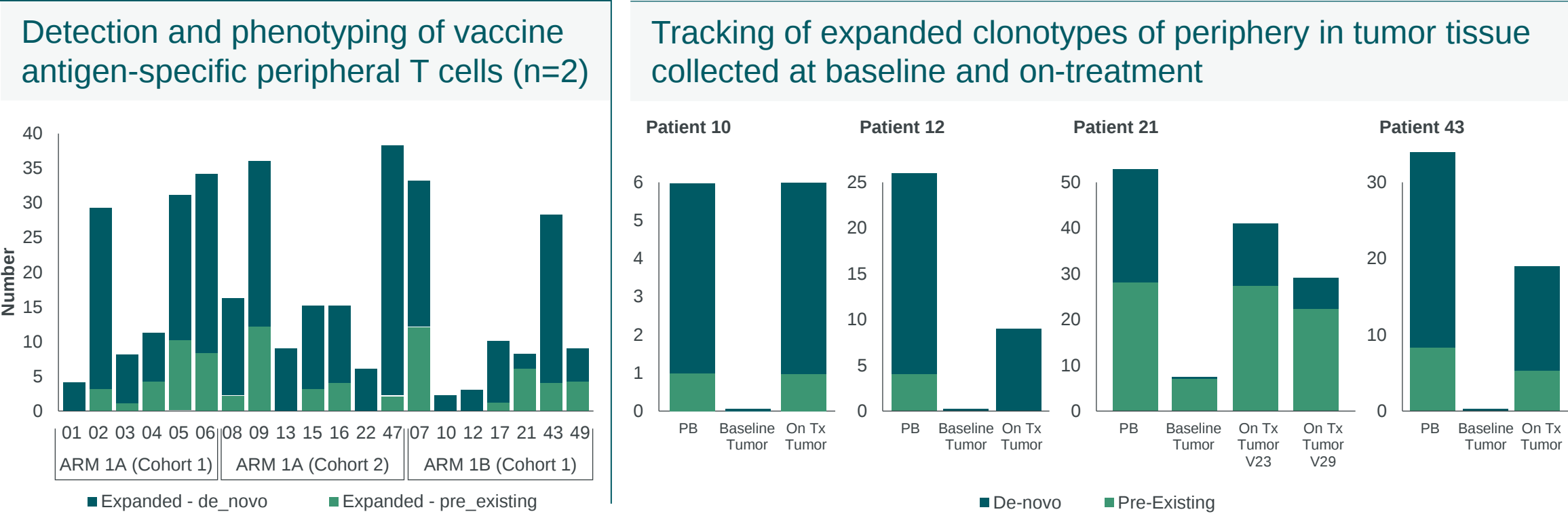
Phenotype of E7 multimer⁺CD8⁺ T cells



Vaccination marked on timeline as vertical grey dotted lines.
At study day 0, <6 multimer events+ were detected in the gate in all samples

- Vaccine-induced CD8⁺multimer⁺: up to 4.98% of CD8 T cells in PBMC
- CD8⁺multimer⁺: effector memory (CD197-CD45RA-) with PD-1 and CD57 expression

BNT113: Kinetic TCR Profiling in PBMC and Tumor



- Expansion of *de novo* and pre-existing TCR clonotypes was observed post vaccination in patients from all three cohorts
- T cell clonotypes expanded in peripheral blood could be tracked in on-treatment (Tx) tumor, but rarely in baseline tumor
- TCRs found in tumor have been validated to be specific-against HPV16 E6/E7¹

1. Data not shown.
Tx = on-treatment.; PV = human papilloma virus; PB = peripheral blood; PBMC = peripheral blood mononuclear cell; TCR = T-cell receptor

BNT113 (HPV16+ carcinomas) – ESMO 2024 Data: Key Takeaway Messages



Safety Profile:

BNT113 – investigational mRNA vaccine encoding HPV16 E6/E7 – was overall well tolerated and had a manageable safety profile



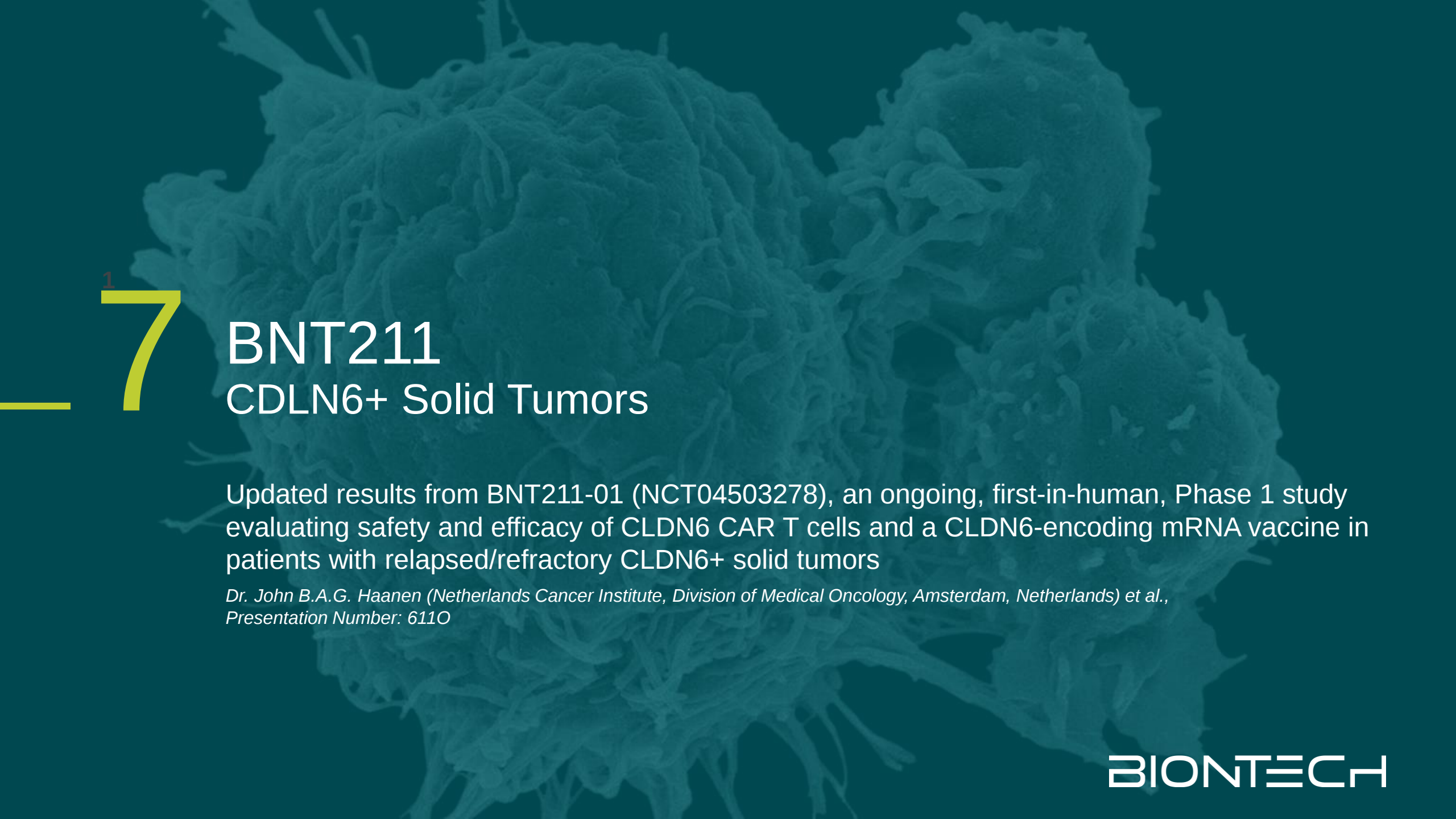
Efficacy:

- T cell induction against both E7 and E6
 - Pre-existing and *de novo* effector T-cell responses were detected *ex vivo* (more pronounced in the adjuvant setting vs advanced disease)
 - Vaccine-induced T cells of effector memory phenotype persisted in circulation beyond treatment period
 - In patients with advanced disease, *de novo* vaccine-induced T cells migrate to tumor post-vaccination
- The vaccine was immunogenic in both the adjuvant and end-stage clinical setting
- In Arm 1B, DCR was 71%



Outlook:

Further studies are needed to fully assess the clinical activity of BNT113

A detailed scanning electron micrograph of a cell cluster, likely a tumor, showing a dense network of cells with numerous protrusions and filaments. The image is rendered in a teal color scheme.

1
7

BNT211

CDLN6+ Solid Tumors

Updated results from BNT211-01 (NCT04503278), an ongoing, first-in-human, Phase 1 study evaluating safety and efficacy of CLDN6 CAR T cells and a CLDN6-encoding mRNA vaccine in patients with relapsed/refractory CLDN6+ solid tumors

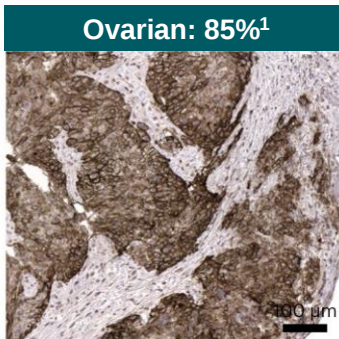
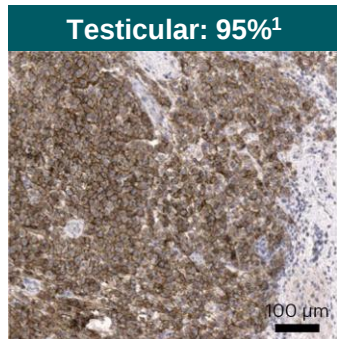
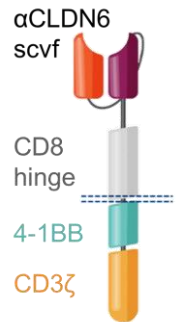
*Dr. John B.A.G. Haanen (Netherlands Cancer Institute, Division of Medical Oncology, Amsterdam, Netherlands) et al.,
Presentation Number: 611O*

BIONTECH

BNT211 – A Potentially First-in-Class Approach for CLDN6+ Solid Tumors

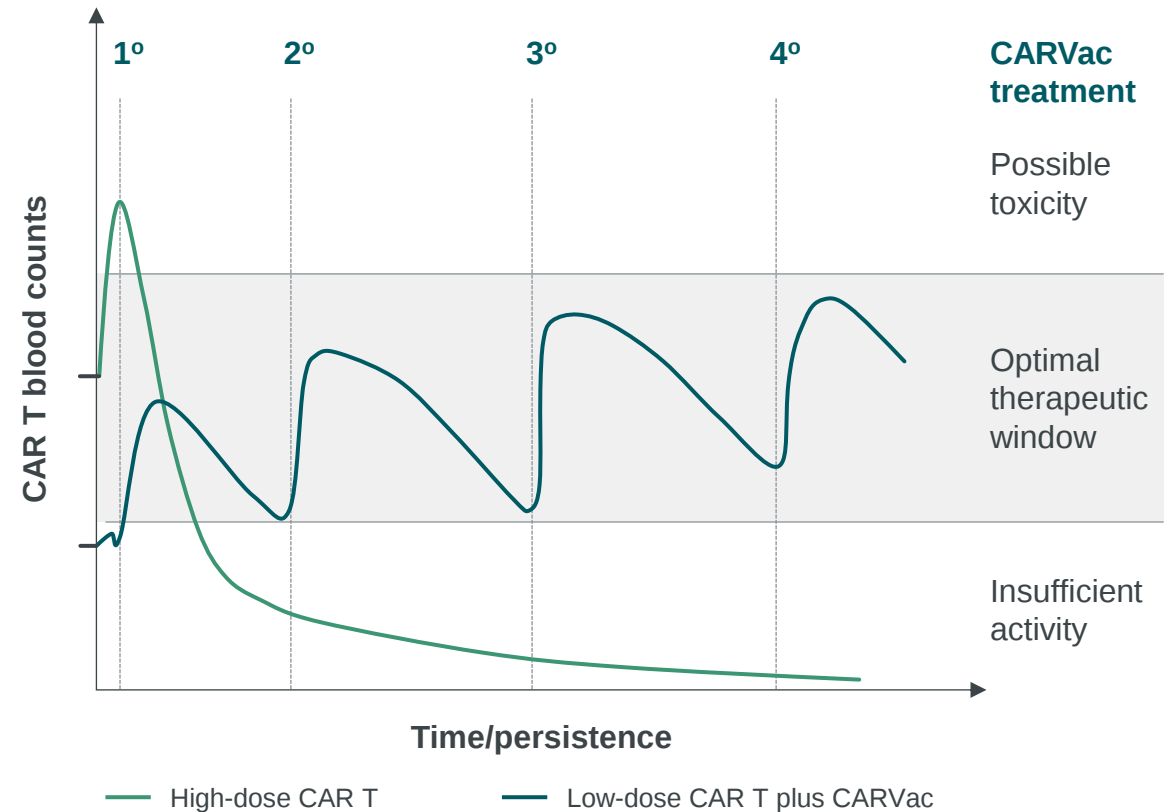
Second generation CAR targeting CLDN6, an oncofetal antigen

CLDN6 CAR T^{1,2} ± CLDN6 CARVac^{3,4}



CLDN6 is an oncofetal antigen, expressed during fetal organogenesis and overexpressed in many solid tumors yet absent in healthy adult tissues¹

Scientific rationale and concept of CARVac-driven expansion of CAR T cells³



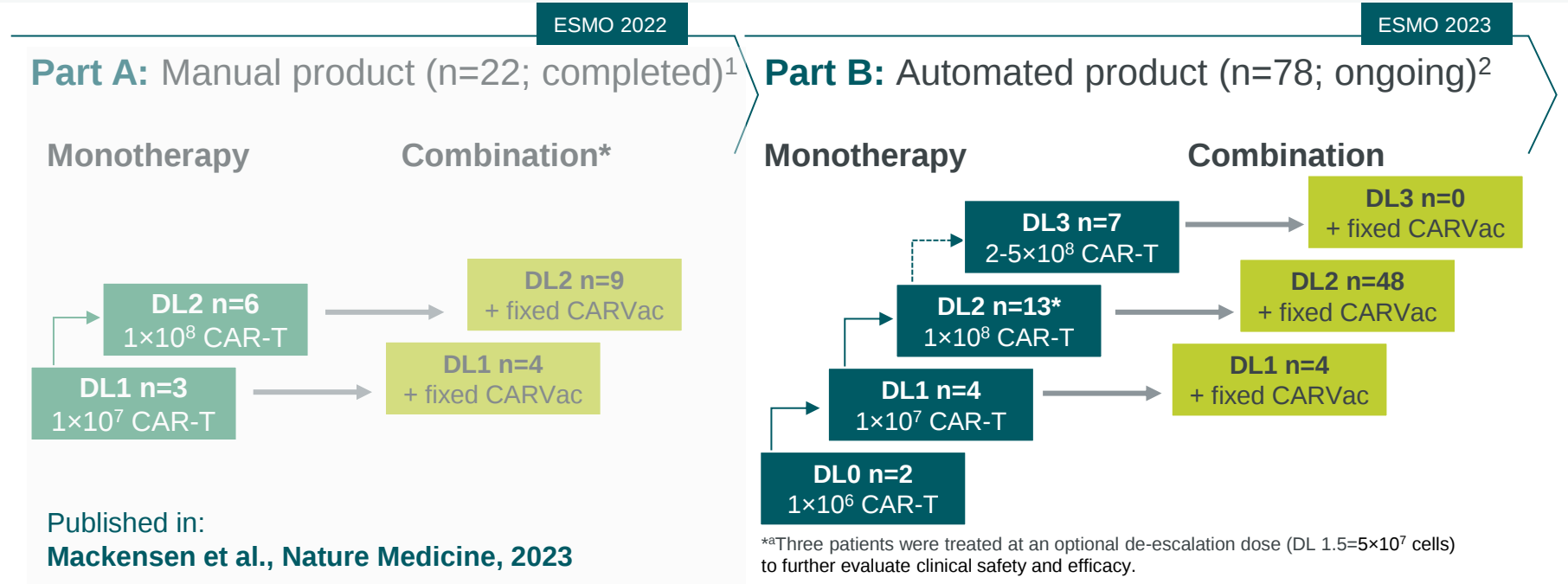
1. Mackensen A, et al. Nature Med 2023;29:2844–2853; 2. Haanen JBAG, et al. Ann Oncol 2023;34 (suppl_2):S1281–S1282; 3. Reinhard K, et al. Science 2020;367:446–453; 4. Sahin U, et al. Nature 2020;585:107–112. CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CD = cluster of differentiation; CLDN6 = Claudin 6; scfv = single-chain variable fragment.

BNT211 as Monotherapy or in Combination with Ribonucleic Acid Lipoplexes (RNA-LPX) in Patients with CLDN6-Positive Advanced Solid Tumors

Phase 1, FIH, open-label, dose escalation study with expansion cohort to evaluate safety and efficacy of BNT211 with/without RNA-LPX in patients with CLDN6+ R/R solid tumors ([NCT04503278](#))

Inclusion criteria

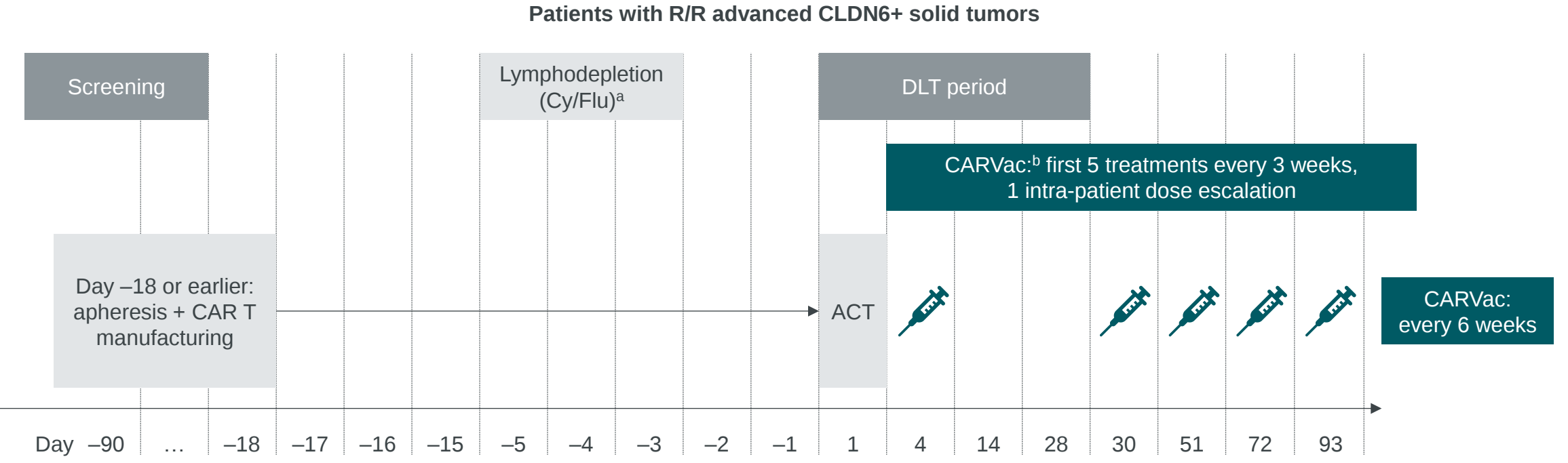
- ≥50% tumor cells with CLDN 6 IHC 2+/3+ CLDN6 positivity (immunohistochemistry)
- Measurable disease per RECIST v1.1 or elevated tumor marker
- ECOG PS 0–1



Dose Escalation Scheme for Automated Cell Product Candidate

Dose escalation was performed with cell products from a **manual** process (n=22; completed)¹ and an **automated** process² (n=78 in the current analysis; ongoing)

Dose escalation scheme for cell product candidate derived from automated process



1. Mackensen A, et al. Nature Med 2023;29:2844–2853; 2. Haanen JBAG, et al. Ann Oncol 2023;34 (suppl_2):S1281–S1282.
aThree patients were treated at an optional de-escalation dose (DL 1.5=5×10⁷ cells) to further evaluate clinical safety and efficacy. bThe starting dose of CARVac dose was 50 µg, with one intra-patient escalation to 100 µg.
ACT = adoptive cell transfer; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; Cy/Flu = cyclophosphamide/fludarabine; DLT = dose limiting toxicity; .

BNT211-01: Baseline Characteristics – Safety Set

Presented are data from N=78 patients who received automated process CAR T

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				
	DL0 (1x10 ⁶)	DL1 (1x10 ⁷)	DL1.5 (5x10 ⁷)	DL2 (1x10 ⁸)	DL3 (2–5x10 ⁸)	DL1 (1x10 ⁷)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	
LD (Flu/Cy)	100%	100%	100%	100%	100%	100%	50%	75%	100%	
Patients, n (%)	(n=2)	(n=4)	(n=3)	(n=10)	(n=7)	(n=4)	(n=6)	(n=15)	(n=27)	
Characteristic										N=78
Median age (range), years	55.5 (50–61)	54.5 (36–62)	46.0 (34–54)	47.5 (30–69)	48.0 (29–63)	51.0 (42–65)	36.0 (26–60)	54.0 (29–68)	46.0 (19–69)	48.0 (19–69)
Female, n (%)	1 (50.0)	1 (25.0)	1 (33.3)	5 (50.0)	3 (42.9)	2 (50.0)	3 (50.0)	8 (53.3)	12 (44.4)	36 (46.2)
CLDN6 2+/3+ cells, %	82.5	97.5	90.0	95.0	90.0	97.5	79.5	90.0	85.0	90.0
Median (range)	(80–85)	(80–100)	(80–95)	(50–100)	(55–100)	(50–100)	(50–100)	(50–100)	(50–100)	(50–100)
Cancer type										
Testicular/GCT ^a	1 (50.0)	0	2 (66.7)	3 (30.0)	3 (42.9)	1 (25.0)	3 (50.0)	7 (46.7)	10 (37.0)	30 (38.4)
Ovarian	1 (50.0)	1 (25.0)	1 (33.3)	5 (50.0)	2 (28.6)	2 (50.0)	2 (33.3)	7 (46.7)	10 (37.0)	31 (39.7)
Sarcoma ^b	0	1 (25.0)	0	0	0	0	1 (16.7)	0	4 (14.8)	6 (7.7)
Lung	0	0	0	2 (20.0)	0	1 (25.0)	0	0	1 (3.7)	4 (5.1)
Esophageal/GEJ	0	2 (50.0)	0	0	1 (14.3)	0	0	0	0	3 (3.8)
Other ^c	0	0	0	0	1 (14.3)	0	0	1 (6.7)	2 (7.4)	4 (5.1)
Median prior lines (range)	3 (2–4)	4 (3–7)	5 (3–6)	3.5 (2–5)	4 (3–5)	4.5 (2–9)	3.5 (2–9)	4 (1–8)	4 (2–11)	4 (1–11)

^a Includes seminoma, non-seminoma, extragonadal GCTs. ^b Includes desmoplastic sarcoma and epitheloid sarcoma. ^c Includes breast cancer, pancreatic cancer, sinusal carcinoma and uterine cancer (n=1 each).

Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; DL = dose level; GCT = germ cell tumor; GEJ = gastro-esophageal junction; LD = lymphodepletion.

BNT211 Showed Consistent Safety Profile1-3 and No Increased Toxicity with Repeated CARVac Administration

With respect to safety results, we observed a CAR-T dose dependency

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				
	DL0 (1x10 ⁶)	DL1 (1x10 ⁷)	DL1.5 (5x10 ⁷)	DL2 (1x10 ⁸)	DL3 (2–5x10 ⁸)	DL1 (1x10 ⁷)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	
LD (Flu/Cy)	100%	100%	100%	100%	100%	100%	50%	75%	100%	
Patients, n (%)	(n=2)	(n=4)	(n=3)	(n=10)	(n=7)	(n=4)	(n=6)	(n=15)	(n=27)	N=78
Any TEAE	2 (100)	4 (100)	3 (100)	10 (100)	7 (100)	4 (100)	6 (100)	15 (100)	27 (100)	78 (100)
Grade ≥3	2 (100)	4 (100)	3 (100)	10 (100)	7 (100)	3 (75.0)	5 (83.3)	13 (86.7)	24 (88.9)	71 (91.0)
Any SAE	1 (50.0)	2 (50.0)	3 (100)	4 (40.0)	4 (57.1)	2 (50.0)	4 (66.7)	9 (60.0)	16 (59.3)	45 (57.7)
Any TRAE ^a	2 (100)	2 (50.0)	3 (100)	10 (100)	7 (100)	4 (100)	5 (83.3)	14 (93.3)	25 (92.6)	72 (92.3)
Grade ≥3 ^a	1 (50.0)	1 (25.0)	3 (100)	10 (100)	6 (85.7)	1 (25.0)	2 (33.3)	9 (60.0)	19 (70.4)	52 (66.7)
Any related SAE	1 (50.0)	-	3 (100)	3 (30.0)	3 (42.9)	-	1 (16.7)	5 (33.3)	10 (37.0)	26 (33.3)
Fatal TEAE	-	-	1 (33.3)	2 (20.0)	1 (14.3)	-	-	1 (6.7)	2 (7.4)	7 (9.0)
Related ^a	-	-	-	2 (20.0)	-	-	-	-	1 (3.7)	3 (3.8)
TEAE leading to treatment discontinuation	-	-	-	-	-	-	-	1 (6.7)	1 (3.7)	2 (2.6)
DLT	-	-	1 (33.3)	1 (10.0)	1 (14.3)	-	-	1 (6.7)	3 (11.1)	7 (9.0)

^a Includes AEs related to CLDN6 CAR T and/or CARVac; does not include events related to LD chemotherapy. Fatal TEAEs related to CAR T ± CARVac included sepsis, fungal pneumonia and HLH (n=1 each). DLTs included HLH/IEC-HS, liver toxicity, cytopenia and CRS.

Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; Cy = cyclophosphamide; DL = dose level; DLT = dose-limiting toxicity; Flu = fludarabine; HLH = hemophagocytic lymphohistiocytosis; IEC-HS = immune effector cell-associated HLH-like syndrome; LD = lymphodepletion; SAE = serious adverse event; TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.

BNT211-01: AEs Associated with CAR T Treatment Class – Safety Set

CRS was mostly grade 1 or 2 (only 2 patients saw Gr 3 or above) and all cases of ICANS were grade 1

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				N=78
	DL0 (1x10 ⁶)	DL1 (1x10 ⁷)	DL1.5 (5x10 ⁷)	DL2 (1x10 ⁸)	DL3 (2–5x10 ⁸)	DL1 (1x10 ⁷)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	DL2 (1x10 ⁸)	
LD (Flu/Cy)	100%	100%	100%	100%	100%	100%	50%	75%	100%	
Patients, n (%)	(n=2)	(n=4)	(n=3)	(n=10)	(n=7)	(n=4)	(n=6)	(n=15)	(n=27)	
CRS ^a Grade 1–2	1 (50.0)	-	2 (66.7)	6 (60.0)	5 (71.4)	2 (50.0)	4 (66.7)	12 (80.0)	18 (66.7)	50 (64.1)
Grade ≥3	-	-	-	-	1 (14.3)	-	-	-	1 (3.7)	2 (2.6)
ICANS Grade 1–2	-	-	-	1 (10.0)	-	-	1 (16.7)	-	1 (3.7)	3 (3.8)
Grade ≥3	-	-	-	-	-	-	-	-	-	-
Any HLH/IEC-HS	-	-	-	2 (20.0)	2 (28.6)	-	-	3 (20.0)	6 (22.2)	13 (16.7)
Grade ≥3	-	-	-	2 (20.0)	2 (28.6)	-	-	1 (6.7)	3 (11.1)	8 (10.3)
Prolonged cytopenias ^b	1 (50.0)	3 (75.0)	3 (100)	6 (60.0)	4 (57.1)	2 (50.0)	1 (16.7)	7 (46.7)	15 (55.6)	42 (53.8)
Anemia	1 (50.0)	1 (25.0)	-	2 (20.0)	1 (14.3)	-	1 (16.7)	2 (13.3)	9 (33.3)	17 (21.8)
Leukopenia	-	-	1 (33.3)	1 (10.0)	1 (14.3)	-	-	-	6 (22.2)	9 (11.5)
Lymphopenia	-	1 (25.0)	-	4 (40.0)	1 (14.3)	2 (50.0)	-	2 (13.3)	5 (18.5)	15 (19.2)
Neutropenia	-	-	-	-	2 (28.6)	-	-	3 (20.0)	-	5 (6.4)
Thrombocytopenia	1 (50.0)	1 (25.0)	1 (33.3)	2 (20.0)	2 (28.6)	1 (25.0)	-	3 (20.0)	5 (18.5)	16 (20.5)
Pancytopenia	-	-	1 (33.3)	1 (10.0)	-	-	-	-	2 (7.4)	4 (5.1)

^a Per American Society for Transplantation and Cellular Therapy (ASTCT) grading guidelines.

^b Grade 3 or 4 cytopenia that has not recovered to Grade ≤ 2 by day 30±2 days after ACT.

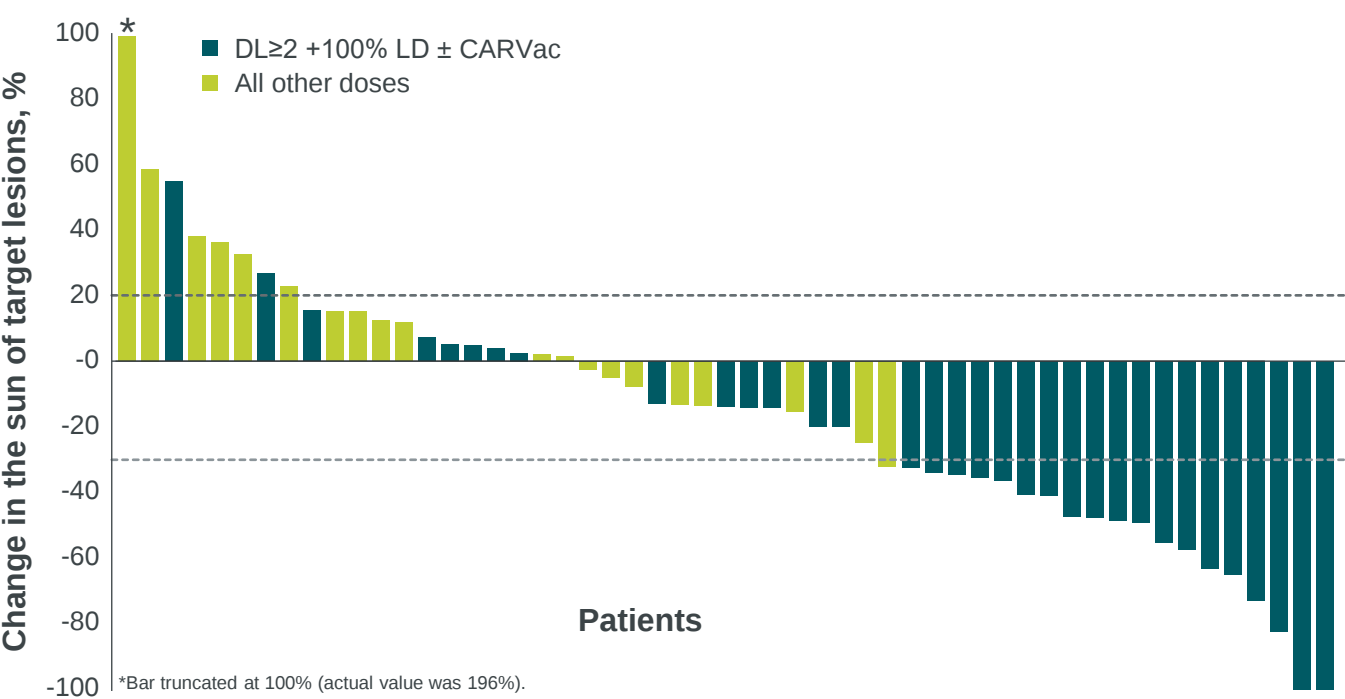
Data cut-off: May 16, 2024.

ACT = adoptive cell transfer; AE = adverse event; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; CRS = cytokine release syndrome; Cy = cyclophosphamide; DL = dose level; Flu = fludarabine; HLH = hemophagocytic lymphohistiocytosis; ICANS = immune effector cell-associated neurotoxicity syndrome; IEC-HS = immune effector cell-associated HLH-like syndrome; LD = lymphodepletion.

BNT211-01: Best Overall Response

Among the 41 patients who received CAR T dose level 2 or dose level 3 (with or without CARvac) - shown below in dark green - ORR and DCR were 51.5% and 84.8%, respectively

Best overall response per RECIST v1.1



Response ^a	Total (N=74) ^b
Evaluable patients, n	64
ORR, n (%)	21 (32.8)
95% CI (%)	18.5–40.1
CR, n (%)	3 (4.1)
PR, n (%)	18 (24.3)
DCR, n (%)	43 (67.2)
95% CI (%)	46.1–69.5

Response ^a	DL≥2 +100% LD ± CARVac (N=41) ^{b,c}
Evaluable patients, n	33
ORR, n (%)	17 (51.5)
95% CI (%)	26.3–57.9
DCR, n (%)	28 (84.8)
95% CI (%)	51.9–81.9

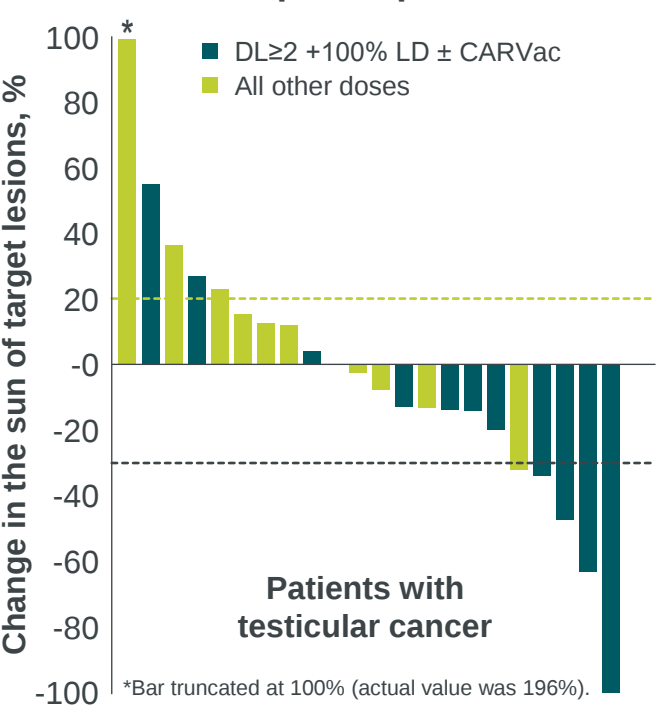
Data cut-off: May 16, 2024.

^a Includes tumor marker responses; ^b Excludes patients who received an out-of-specification product; ^c DL2=1×10⁸; DL3=2–5×10⁸ CAR T cells.
ACT = adoptive cell transfer; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI = confidence interval; CR = complete response; DCR = disease control rate; DL = dose level; LD = lymphodepletion;
ORR = objective response rate; PR = partial response.

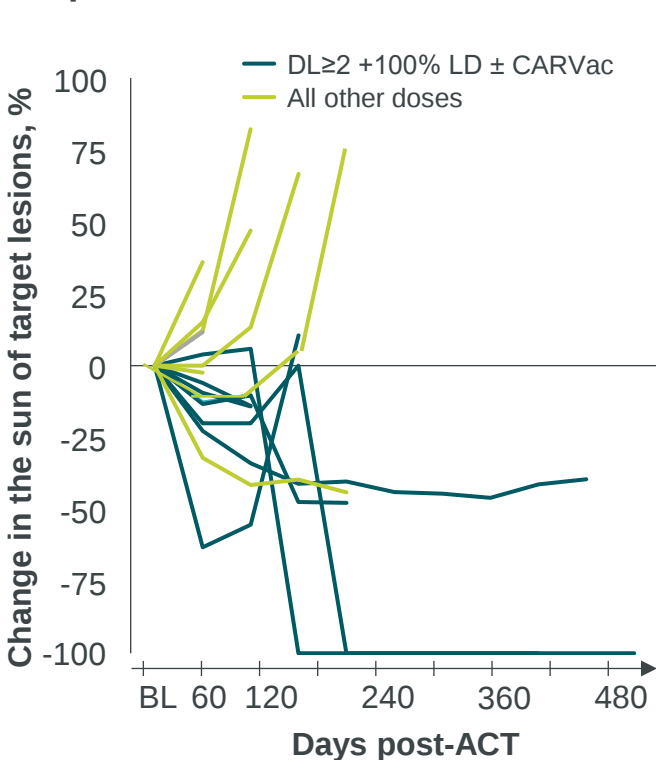
BNT211-01: Overall Response Rate – Testicular Cancer

In this patient group, overall response rate was 24%; at DL2 and DL3 ORR was 41.7%. Two patients had a surgical complete response that lasted for over a year

Best overall response per RECIST v1.1



Response over time



Response ^a	Total (N=27) ^b
Evaluable patients, n	25
ORR, n (%)	6 (24.0)
95% CI (%)	8.6–42.3
DCR, n (%)	14 (56.0)
95% CI (%)	32.0–71.3

Response ^a	DL≥2 +100% LD ± CARVac (N=14) ^{b,c}
Evaluable patients, n	12
ORR, n (%)	5 (41.7)
95% CI (%)	12.8–64.9
DCR, n (%)	9 (75.0)
95% CI (%)	35.1–87.2

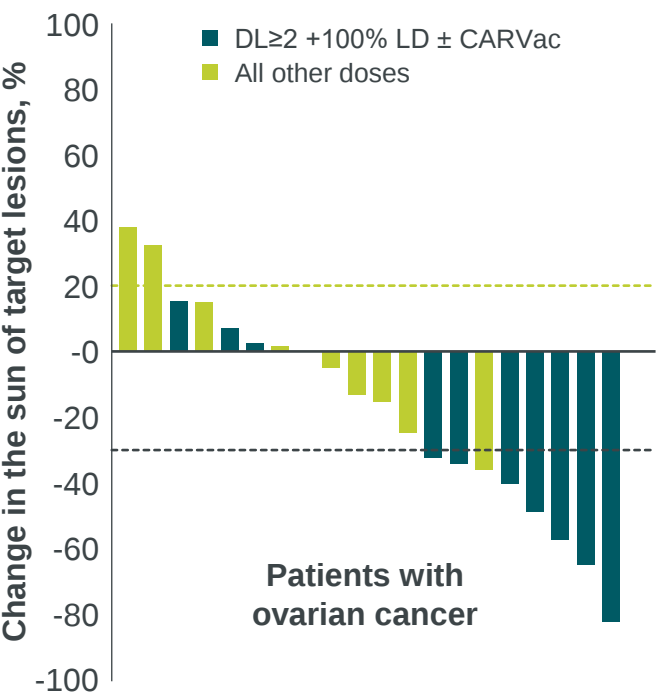
a. Includes tumor marker responses; b. Excludes patients who received an out-of-specification product; c. DL2=1×10⁸; DL3=2–5×10⁸ CAR T cells.
ACT = adoptive cell transfer; BL = baseline; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI = confidence interval; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate.

Data cut-off: May 16, 2024.

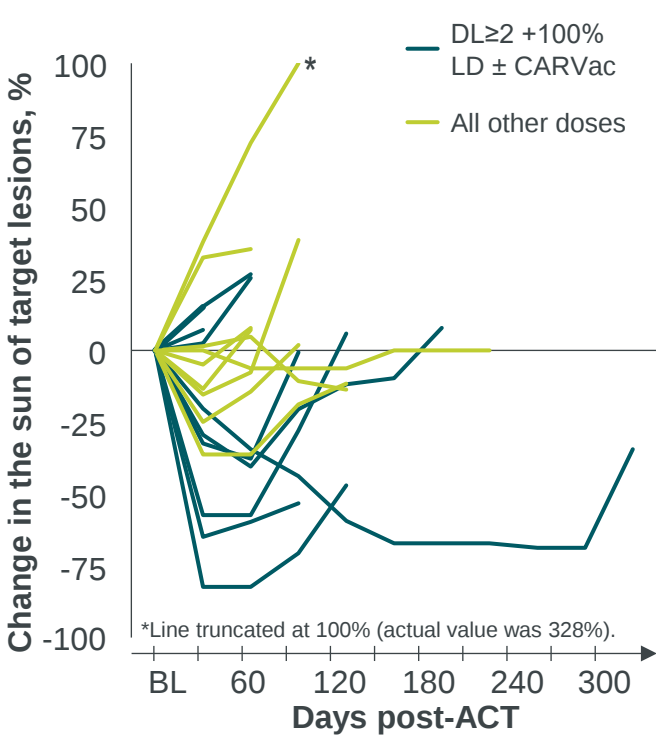
BNT211-01: Overall Response Rate – Ovarian Cancer

Of the 24 evaluable patients across all DLs we see ORR was 33.3% while DCR was 75% - the same parameters when considered for DL2 and above are 58.3% and 83.3% respectively

Best overall response per RECIST v1.1



Response over time



Response ^a	Total (N=30) ^b
Evaluative patients, n	24
ORR, n (%)	8 (33.3)
95% CI (%)	12.3–45.9
DCR, n (%)	18 (75.0)
95% CI (%)	40.6–77.3

Response ^a	DL≥2 +100% LD ± CARVac (N=16) ^{b,c}
Evaluative patients, n	12
ORR, n (%)	7 (58.3)
95% CI (%)	19.8–70.1
DCR, n (%)	10 (83.3)
95% CI (%)	35.4–84.8

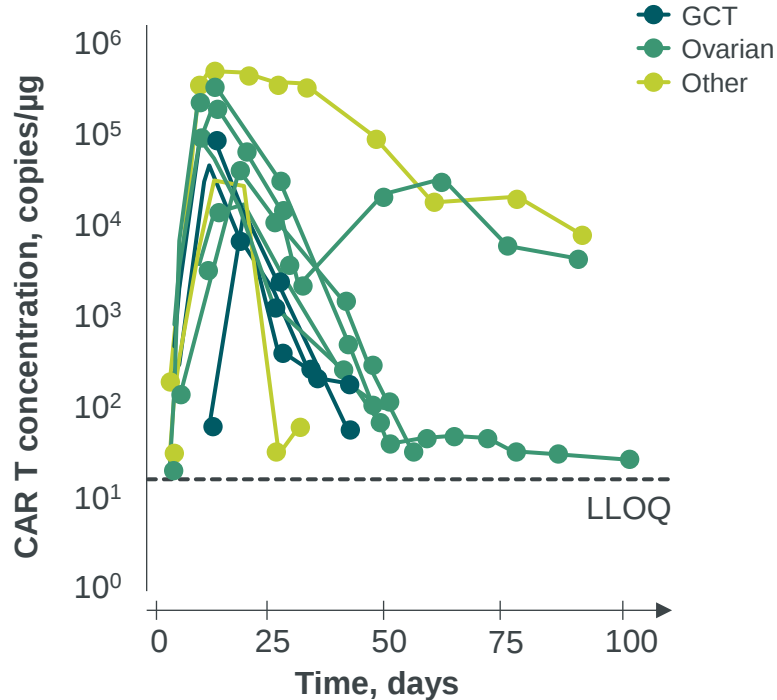
Data cut-off: May 16, 2024.

a. Includes tumor marker responses; b. Excludes patients who received an out-of-specification product; c. DL2=1×10⁸; DL3=2–5×10⁸ CAR T cells.
ACT = adoptive cell transfer; BL = baseline; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI = confidence interval; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate.

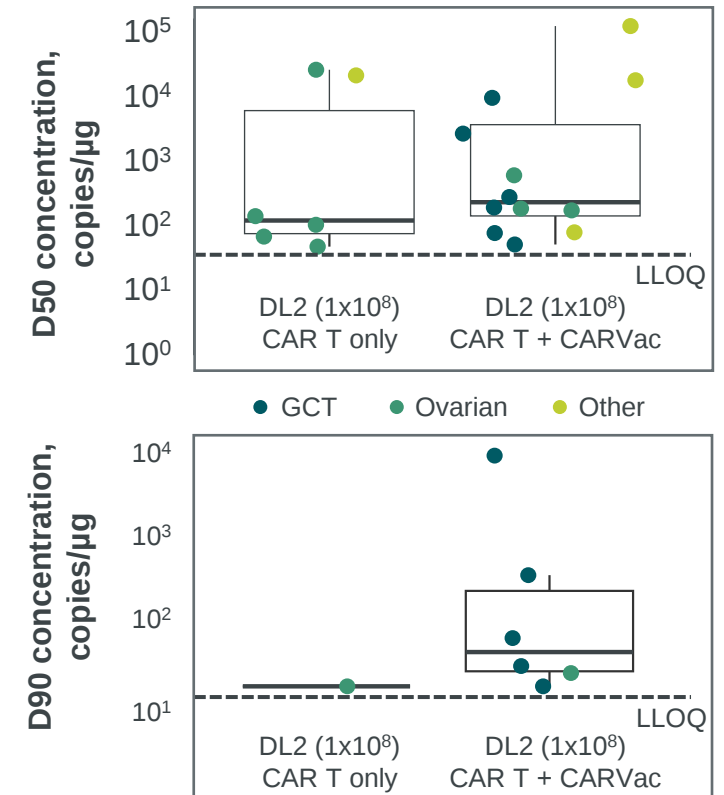
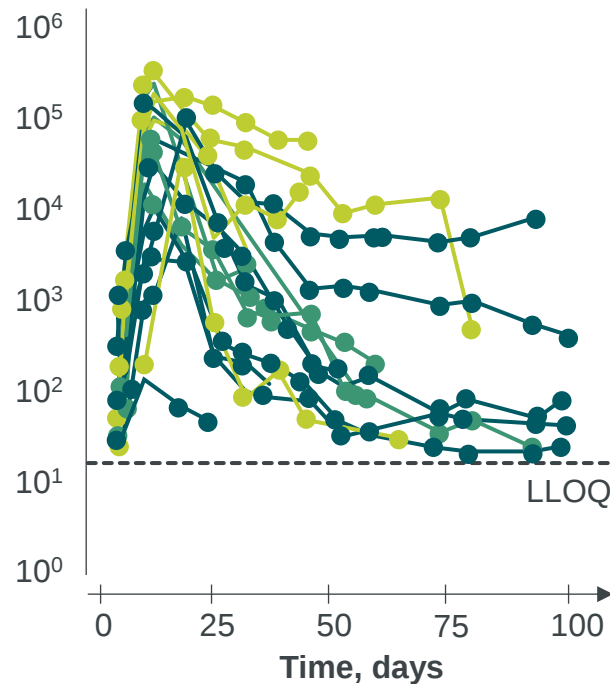
BNT211-01: At DL2, CARVac Improved CAR T Persistence Beyond 100 Days

Adding CARVac limits the decline and induces a plateau of CAR-T cells with robust and ongoing detection for several additional weeks in nearly all patients who received DL2+CARVac

DL2 (1×10^8) CAR T alone



DL2 (1×10^8) CAR T + CARVac



Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI = confidence interval; CLDN6 = claudin 6; DL = dose level; GCT = germ cell tumor.

BNT211 – ESMO 2024 Data: Key Takeaway Messages



Safety Profile:

The safety profile of the investigational therapy CLDN6 CAR T cells ± CARVac was consistent with the previously published effect of CAR T therapies;^{1–3} repeated CARVac administration did not result in increased toxicity



Efficacy:

Encouraging signs of antitumor activity across all indications, especially in patients with germ cell tumors/ testicular cancer and ovarian cancer:

- Among patients who received DL≥2 +100% LD ± CARVac, ORR^a was 41.7% (testicular) and 58.3% (ovarian)
- Three patients experienced durable responses that lasted over a year (2 CRs, 1 PR)

CARVac improved CAR T persistence beyond 100 days



Outlook:

Follow up is ongoing. The study will evaluate the safety and tolerability of DL3 + CARVac

1. Shah NN, et al. J Clin Oncol 2020; 38(17):1938–1950; 2. Hines MR, et al. Br J Haematol 2021;194(4):701–707; 3. Liechtenstein DA, et al. Blood 2021;138(24):2469–2484; Hines MR, et al. Transplant Cell Ther 2023;29(7):438.e1–438.e16.
a. Includes tumor marker responses; DL2=1×10⁸; DL3=2–5×10⁸ CAR T cells.
CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CR = complete response; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate; PR = partial response.

¹
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BNT323 / DB-1303¹ HER2-low Breast Cancer

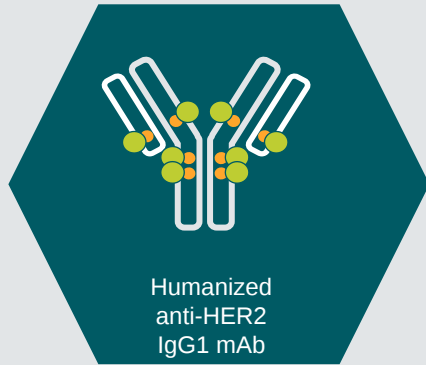
DYNASTY-Breast02: A Phase 3 trial of BNT323/DB-1303 vs Investigator's Choice
Chemotherapy in HER2-low, Hormone Receptor Positive, Metastatic Breast Cancer

Joyce O'Shaughnessy (Baylor University Medical Center, Texas Oncology, US Oncology Dallas, TX, USA) et al.; Presentation Number: 436TiP

1. Partnered with Duality Biologics

BIONTECH

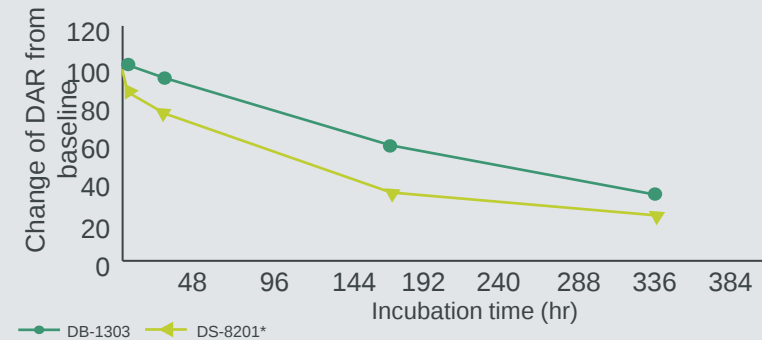
BNT323/DB-1303¹: A HER2 ADC with a Potentially Differentiated Profile



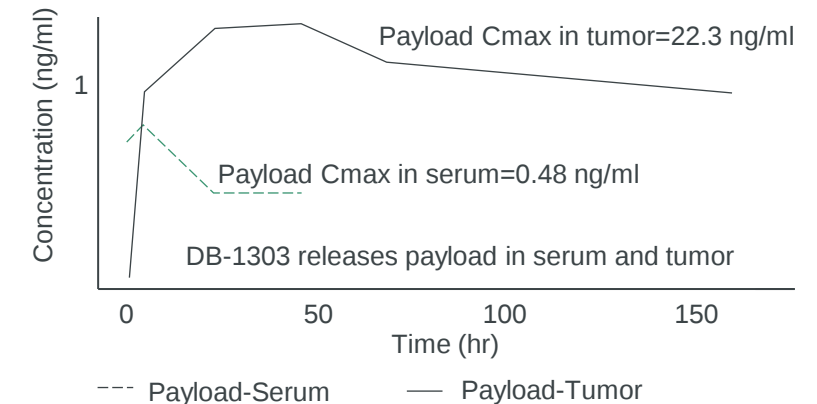
- A humanized anti-HER2 IgG1 mAb, with a wild-type Fc
- A proprietary DNA topoisomerase I inhibitor (P1003)
- A maleimide tetrapeptide-based tumor-selectively cleavable linker (L101)
- High drug-to-antibody ratio: ~8

Lin S. et al. Abstract #252. Presented at EORTC-NCI-AACR in 2022.

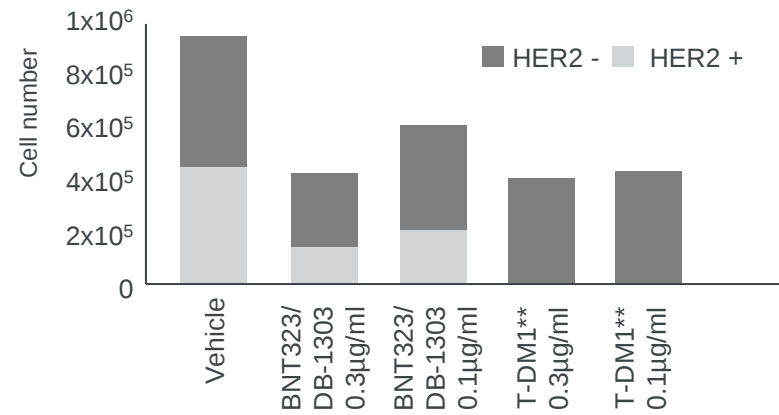
Superior *in vitro* plasma stability in human plasma



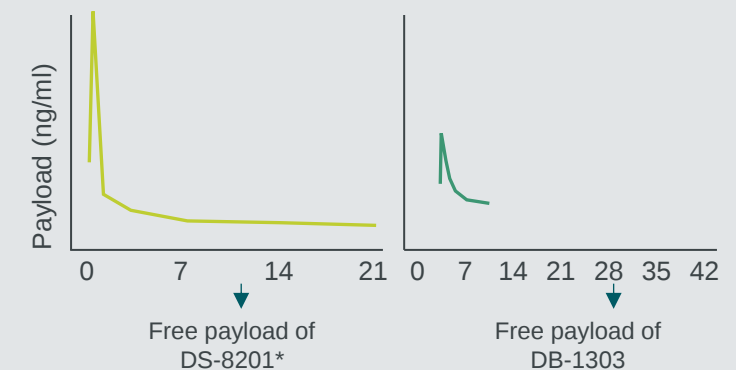
Sustained tumor-selective drug release in tumor-bearing mice



Efficient bystander killing in tumor cell lines



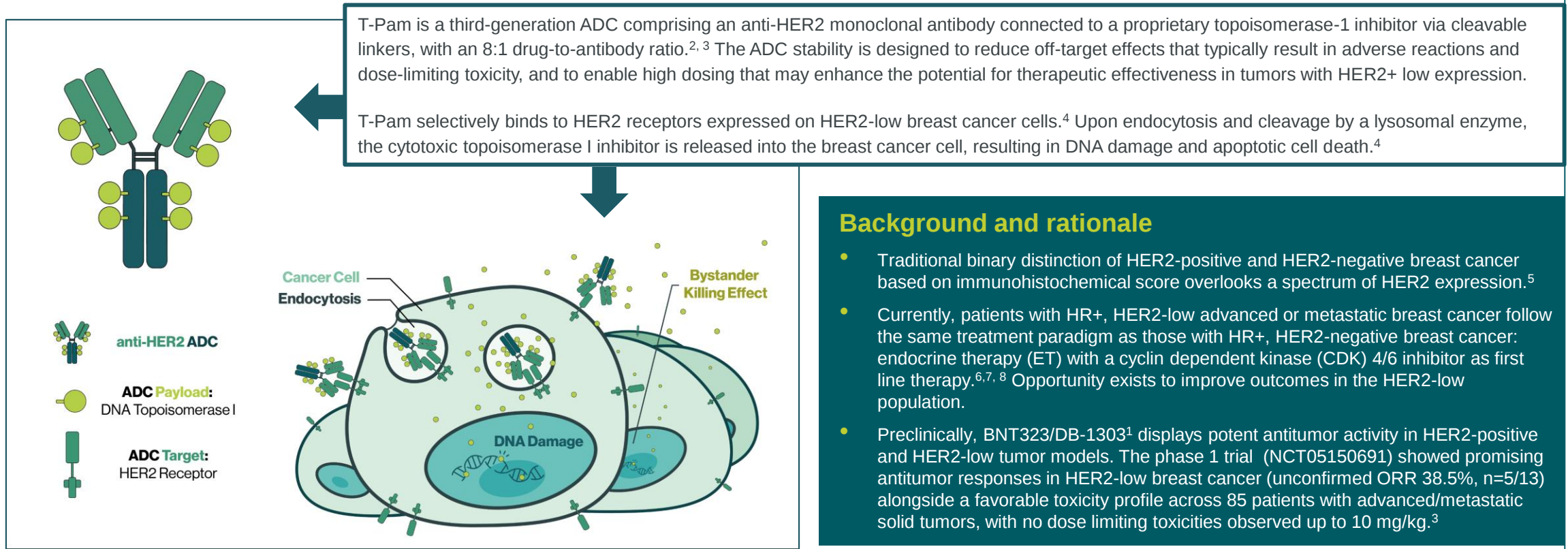
Rapid systemic clearance in monkeys



¹.Partnered with DualityBio. *DS-8201 is an in-house produced analog of DS-8201, Trastuzumab deruxtecan; **Trastuzumab-Emtansin.
ADC = Antibody-drug conjugate; cmax = maximum concentration; DAR = Drug antibody ratio. HER = human epidermal growth factor receptor.

BNT323/DB-1303¹ Proposed Mechanism of Action

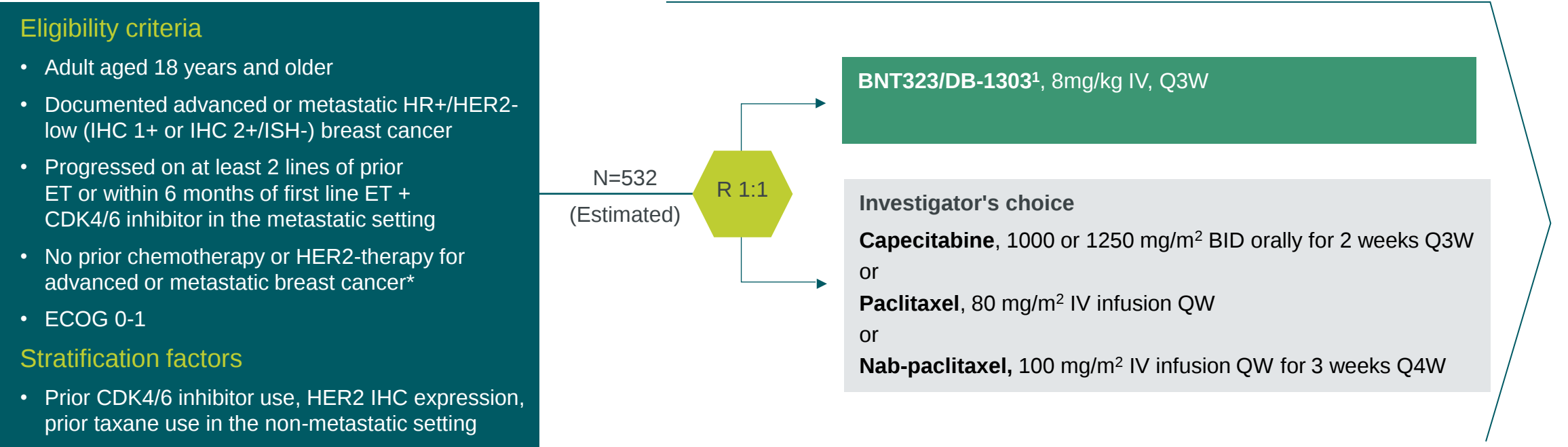
A humanized anti-HER2 IgG1 monoclonal antibody, conjugated to a DNA topoisomerase I inhibitor via a cathepsin-cleavable maleimide tetrapeptide (GGFG) linker with a drug-to-antibody ratio of ~8:1^{2,3}



1. Partnered with Duality Bio; 2. Lin S, et al. Eur J Cancer. 2022; 174, S91. doi: [https://doi.org/10.1016/S0959-8049\(22\)01039-5](https://doi.org/10.1016/S0959-8049(22)01039-5); 3. Moore K, et al. J Clin Oncol 41, 2023; suppl 16; abstr 3023. doi: https://doi.org/10.1200/JCO.2023.41.16_suppl.3023; 4. Metrangola V, Engelholm LH. 2024; 16(2):447. doi: <https://doi.org/10.3390/cancers16020447>; 5. Molinelli Cet al., ESMO Open. 2023 Aug;8(4):101592. doi: 10.1016/j.esmoop.2023.101592; 6. Gennari A et al., Ann Oncol. 2021; 32: 1475–1495; 7. Gradishar WJ et al., J Natl Compr Cancer Netw. 2022; 20: 691–722; 8. Wang X. et al. Cancer Gene Ther 2024. <https://doi.org/10.1038/s41417-024-00747-x>. ADC = antibody drug conjugate; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; ORR = overall response rate.

BNT323/DB-1303¹ Phase 3 Trial in CTx-Naïve Patients with HR+/HER2-Low Breast Cancer who progressed after 2 ET therapies (DYNASTY-Breast02)

Phase 3, randomized, multi-center, open-label study of BNT323/DB-1303¹ (trastuzumab pamirtecan) versus investigator's choice chemotherapy in HER2-Low, HR+ metastatic breast cancer ([NCT06018337](#))





Endpoints

Primary: PFS by BICR according to RECIST 1.1

Secondary: OS, ORR, DoR, DCR, TEAEs and SAEs, PRO, PK

Exploratory: PK, ADA prevalence and incidence, DCR, TTR, PFS2, TFST, TSST, Patient-reported treatment tolerability

1. Partnered with DualityBio; 2. Gennari A et al., Ann Oncol. 2021; 32: 1475– 1495. * Subjects who have received chemotherapy in the neo-adj. or adj. setting are eligible, as long as they have had a disease-free interval (defined as completion of systemic chemotherapy to diagnosis of adv. or met disease) of >12 months. ADA = antibody drug antibody; CTx = chemotherapy; DCR = disease control rate; DoR = duration of response; HR = hormone receptor; ECOG = eastern Cooperative oncology group; ET = endocrine therapy; HER = human epidermal growth factor; IV = intravenous; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PK = pharmacokinetics; PRO = patient reported outcome; QXW = every X weeks; RECIST = response evaluation criteria in solid tumors; SAE = severe adverse event TTR = time to response; TF/SST = time to first/second subsequent treatment or death.

BNT323/DB-1303¹ Evaluated in a Global, Multi-Center, Phase 3 Trial (DYNASTY-Breast02)

Planned study sites

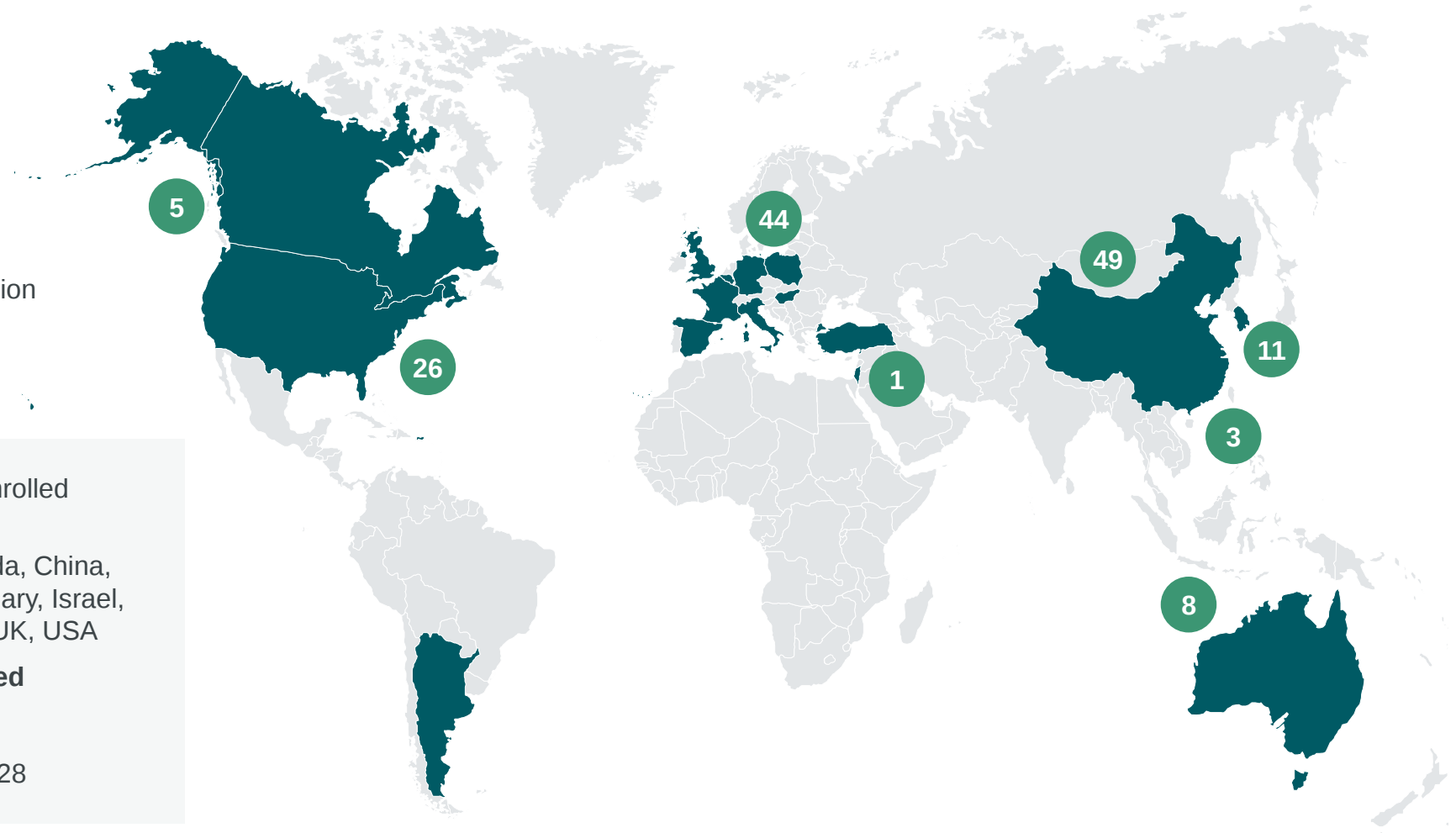
- Countries with planned sites
- Number of initiated sites in each region (correct at time of print)

Approximately 532 patients will be enrolled across the following countries:

- Argentina, Australia, Belgium, Canada, China, France, Germany, Hong Kong, Hungary, Israel, Italy, Korea, Poland, Spain, Turkey, UK, USA
- A total of **147 sites currently initiated**

First patient in: January 2024

Estimated study completion: May 2028



¹. Partnered with DualityBio;

¹
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BNT314 / GEN1059¹

Malignant Solid Tumors

Phase 1/2 dose escalation/expansion trial to evaluate safety and preliminary efficacy of DuoBody-EpCAMx4-1BB (BNT314/GEN1059) alone or in combination with an immune checkpoint inhibitor in patients with malignant solid tumors

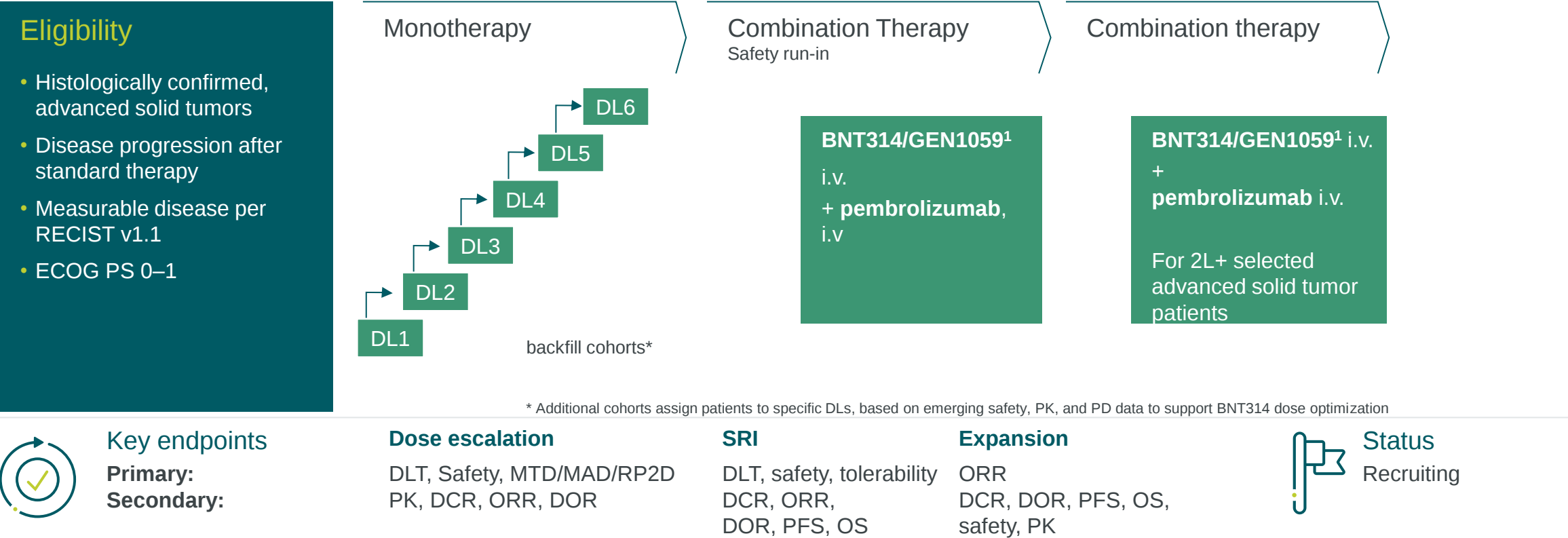
I. Melero , Presentation Number: 1072TiP

1. Partnered with Genmab

BIONTECH

BNT314/GEN1059¹ as Monotherapy or in Combination with Immune Checkpoint Inhibitor in Patients with Malignant Solid Tumors

Phase 1/2, FIH, open-label, dose escalation and expansion trial to evaluate safety of BNT314/GEN1059¹ alone or in combination with pembrolizumab in patients with different types of cancer ([NCT06150183](#))



1. Partnered with Genmab; . ADA = anti-drug antibody; DCR = disease control rate; DL = dose level; DLT = dose limiting toxicity; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; FIH = first in human; iMAD = maximal administered dose; MTD, maximal tolerated dose; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PK = pharmacokinetics; RECIST = Response Evaluation Criteria in Solid Tumors; RP2D = recommended phase 2 dose; TEAEs = treatment emergent adverse events.

BNT314/GEN1059¹: Proposed Mechanism of Action

BNT314/GEN1059¹ (DuoBody-EpCAM×4-1BB) is an investigational bispecific antibody designed to enhance T-cell activation in the tumor microenvironment by targeting 4-1BB and EpCAM.

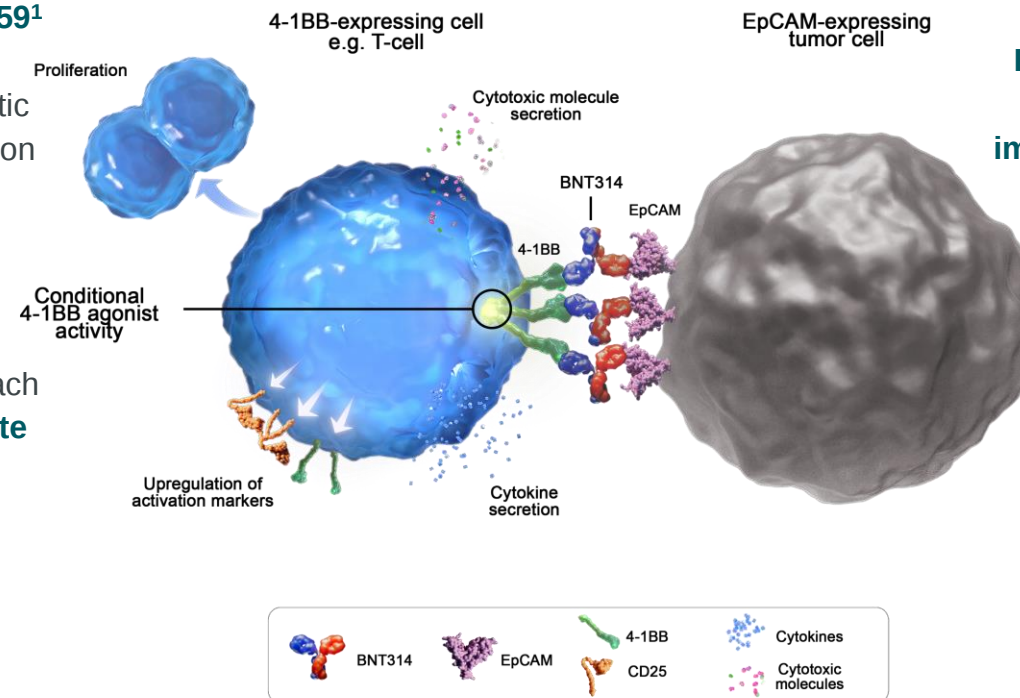
Background and rationale

- While PD-(L)1 inhibitors have marked an advancement in immuno-oncology, the response to such treatments varies among patients, and not all responders sustain long-term benefits, highlighting an ongoing unmet medical need in patients with advanced solid tumors^{2,3}. Furthermore, the therapeutic potential of 4-1BB agonists has been recognized in immuno-oncology⁴⁻⁶.
- Preclinical studies showed that BNT314/GEN1059¹ conditionally enhanced activation and proliferation of T cells, cytokine secretion, and cytotoxic activity. Furthermore, proof-of-principle studies showed antitumor activity of an Fc-silent EpCAM×4-1BB bispecific antibody in mice⁷.

BNT314/GEN1059¹

is Fc-silenced. Its 4-1BB agonistic activity depends on **simultaneous binding to EpCAM**.

This conditional activation approach aims to **potentiate the immune response** at the tumor site, while **minimizing systemic exposure**.



The combination of **BNT314/GEN1059¹** with established **immune checkpoint inhibitors** like pembrolizumab is hypothesized to **amplify antitumor immunity**.

1. Partnered with Genmab; 2. Galon, J. and D. Bruni, Nat Rev Drug Discov, 2019. 18(3); 3. Jenkins, R.W., D.A. Barbie, and K.T. Flaherty, Br J Cancer, 2018. 118(1); 4. Chester, C., et al., Blood, 2018. 131(1); 5. Kim, A.M.J., M.R. Nemeth, and S.-O. Lim, Frontiers in Oncology, 2022. 12; 6. Melero, I., et al., Cancer Discovery, 2023. 13(3); 7. Fellermeier-Kopf, S., et al., 1072P. Annals of Oncology, 2023. 34
CD25 = cluster of differentiation 25; EpCAM = epithelial cell adhesion molecule; Fc = tail region of an antibody that interacts with cell surface receptors (e.g. 4-1BB or EpCAM); PD-L1 = programmed cell death ligand 1;

BNT314/GEN1059¹ Evaluated in a Global, Multi-Center, Phase I/II Trial

Active and planned study sites

■ Active sites

● Planned sites*

* Additional countries to be included for the expansion part

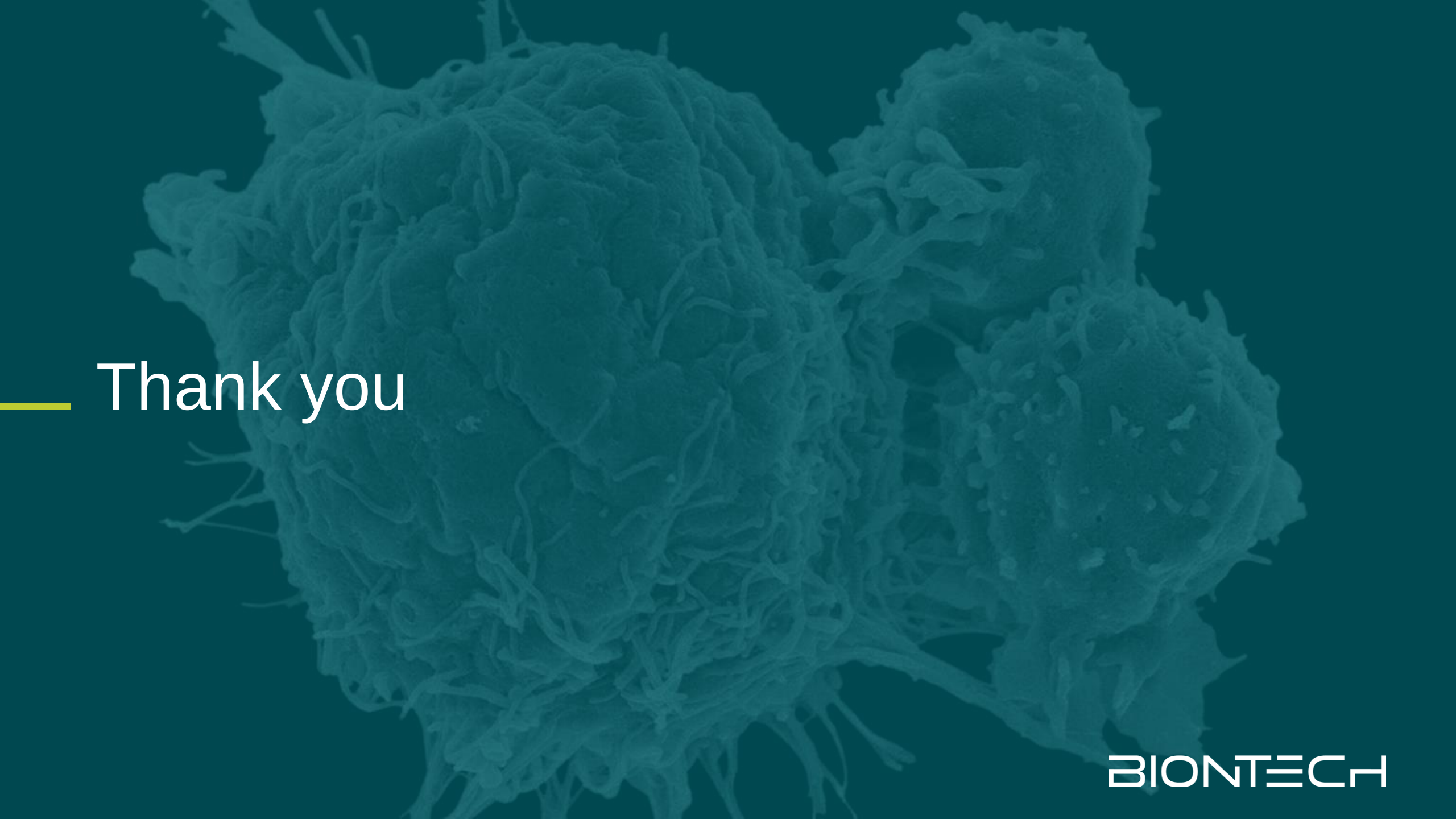
Approximately 360 patients will be enrolled across the following countries:

- Belgium, Spain, United Kingdom, USA as well as additional countries to be included such as Japan and Denmark.

First patient in: Jan 2024



1. Partnered with Genmab.

A scanning electron micrograph (SEM) of a cell cluster, likely a tumor spheroid, showing a dense, irregular mass of cells with many fine, hair-like projections (microvilli) extending from the surface. The image is rendered in a teal color scheme.

— Thank you

BIONTECH