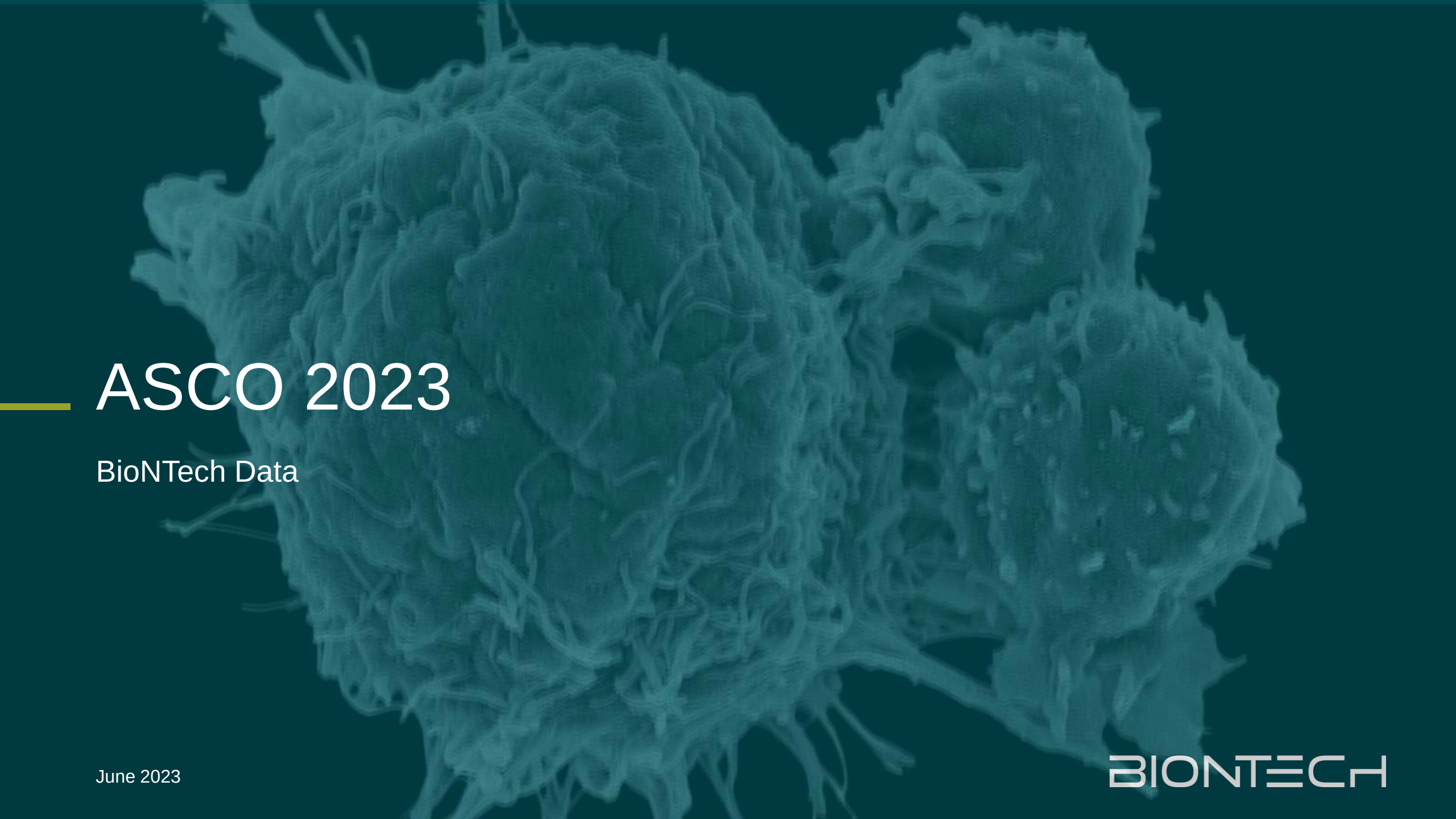


ASCO 2023

BioNTech Data

June 2023

Oncology Pipeline

Drug Class	Phase 1 (5 First-in-Human)	Phase 1/2	Phase 2
mRNA	**BNT111** Advanced melanoma	**BNT112** Prostate cancer	**BNT111** aPD1-R/R melanoma, + Pembrolizumab
	BNT116 2L NSCLC	**BNT113**[1] HPV16+ head and neck cancer	**BNT113** 1L rec./met. HPV16+ PDL1+ head and neck cancer, + Pembrolizumab
	Autogene cevumeran (BNT122)[2] Multiple solid tumors	**BNT141** (CLDN18.2) Multiple solid tumors	**Autogene cevumeran (BNT122)**[2] 1L Adv. melanoma, + Pembrolizumab
	BNT131 (SAR441000)[3] Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)	**BNT142** (CLDN6) Multiple solid tumors	**Autogene cevumeran (BNT122)**[2] Adjuvant colorectal cancer
	BNT152 + BNT153 Multiple solid tumors (IL-7, IL-2)	**BNT151** (IL-2 variant) Multiple solid tumors	
Cell therapy	**BNT221** Refractory metastatic melanoma	**BNT211** (CLDN6) Multiple solid tumors	
Protein-based Therapeutics	**BNT321** Pancreatic cancer (sLea)	**BNT311 (GEN1046)**[4] (PD-L1x4-1BB) Multiple solid tumors	**BNT311 (GEN1046)**[4] (PD-L1x4-1BB) aPD1-R/R NSCLC, + Pembrolizumab
	BNT322 (GEN1056)[4] Multiple solid tumors (undisclosed)	**BNT312 (GEN1042)**[4] (CD40x4-1BB) Multiple solid tumors	**BNT316 (ONC-392)**[5] (CTLA-4) Plat.-R ovarian cancer, + Pembrolizumab
		BNT313 (GEN1053)[4] (CD27) Multiple solid tumors	
		BNT316 (ONC-392)[5] (CTLA-4) Multiple solid tumors	
		BNT323 (DB-1303)[6] (HER2) Multiple solid tumors	
SMIM		**BNT411** (TLR7) Multiple solid tumors	

1. Investigator-initiated / Investigator-initiated and sponsored trial; 2. Partnered with Genentech, member of Roche Group; 3. Partnered with Sanofi; 4. Partnered with Genmab; 5. Partnered with OncoC4; 6. Partnered with DualityBio.
NSCLC = Non-small cell lung cancer; HPV = Human papillomavirus; CLDN = Claudin; IL = Interleukin;1L = first line; TLR = Toll-like receptor; R/R = Relapsed/Refractory; Plat.-R. = Platinum-resistant; ADC = Antibody-drug conjugate; SMIM = small molecule immunomodulator.

BIONTECH

1

BNT316 (ONC-392)

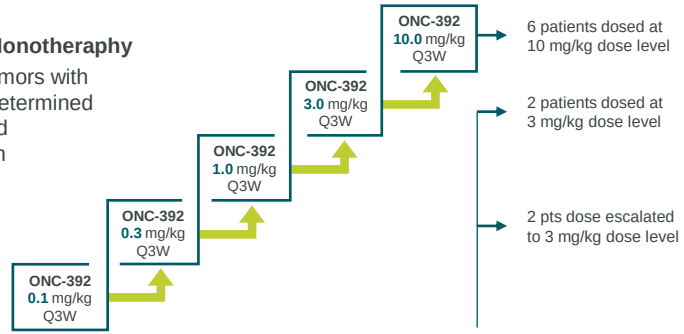
Safety and clinical activity of target-preserving anti-CTLA-4 antibody ONC-392 as Monotherapy in NSCLC patients who progressed on PD(L)1-targeted immunotherapy

MoA Designed to Allow Higher Dosing & Longer Duration of Treatment with ONC-392
PRESERVE-001: Study Design and Safety (NCT04140526)

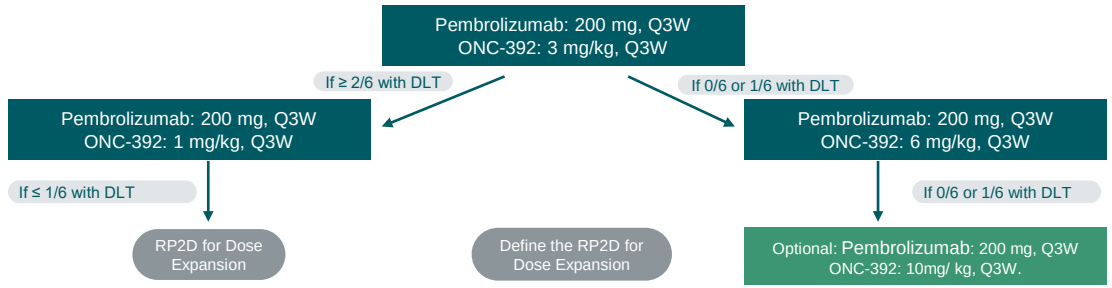
Monotherapy: Dose Finding
(Li T. et al. Poster #949, Presented at SITC 2021)

Objective: To estimate MTD or RP2D for Monotheraphy

Patients with advanced or metastatic solid tumors with measurable or non-measurable disease as determined by RECIST version 1.1, who have progressed despite standard of care therapy, or for whom no standard therapies exist



Combination: Dose Escalation
(Hu-Lieskovan et al. Poster #594. Presented at SITC 2022)



Dose expansion tested in multiple cancer types including:

IO naive NSCLC	IO R/R NSCLC	IO naive Melanoma	IO R/R Melanoma

Safety data and study conclusions

- ONC-392 dosed as mono-therapy and in combination with pembrolizumab were well tolerated
  - TRAE were manageable, no DLTs, MTD not reached
  - Monotherapy RP2D: 10 mg/kg, Combination RP2D: 6 mg/kg
- Preliminary data demonstrated lower irAE rate than observed for comparable IO or IO-IO combinations
- Safety profile of ONC-392 allows for higher dosing and longer duration of treatment in monotherapy and in combination with pembrolizumab

Q3W = Every three weeks; MTD = Maximum tolerated dose; RP2D = Recommended phase 2 dose; DLT = Dose-limiting toxicity; TRAE = Treatment related adverse event; NSCLC = Non-small cell lung cancer; irAE = immune-related adverse event, IO = immuno-oncologic, R/R = relapsed/refractory

BIONTECH

BNT316 (ONC-392): Patient characteristics and Safety

Demographics and Safety Data Summary

Categories	Data (Date Cutoff date: 03/10/2023)
Patients enrolled	35
Median age (range) [Q1, Q3]	66 (43 - 89) [60, 75]
Gender	15F (43%), 20M (57%)
Race (white/Black	33/2
Ethnicity (Hispanic or Latino)	2
Cohorts	
Part A: NSCLC, PD-1 R/R, 10 mg/kg, q3w	2
Arm I: NSCLC, PD-1 R/R, 10 mg/kg x 2, then 6 mg/kg, q3w	33
Non-squamous cell carcinoma	20 (57%)
Squamous cell carcinoma	15 (43%)
ECOG score	
ESCG = 0	9 (26%)
ESCG = 1	26 (74%)
Have Metastatic Lesions	35 (100%)
ONC-392 related AE (TRAE): All grades	26 (74%)
TRAE: Grade 3-4	15 (43%)
irAEs: all grades	19 (54%)
irAE: Grade 3-4	12 (34%)
TRAE: Grade 3 and 4	
TRAE leading to dose interruption	9 (26%)
TRAE leading to dose reduction	1 (3%)
TRAE leading to study drug discontinuation	7 (20%)

System Organ Class	All Grades (≥2 cases)	Grade 3	Grade 4
Preferred Term	N (%)	N (%)	N (%)
Gastrointestinal disorders			
Diarrhea	5 (14%)	1 (3%)	0
Colitis	4 (11%)	3 (9%)	0
Nausea	2 (6%)	1 (3%)	0
Vomiting	3 (9%)	1 (3%)	0
General disorders an administration site conditions			
Fatigue	4 (11%)	1 (3%)	0
Chills	4 (11%)	0	0
Pyrexia	3 (9%)	0	0
Skin and subcutaneous tissue disorders			
Rash maculo-popular	0	0	0
Pruritus	2 (6%)	0	0
Rash	2 (6%)	0	0
Injury, poisoning and procedural complications			
Infusion related reaction	7 (20%)	0	0
Investigations			
AST/ALT increased	6 (17%)	1 (3%)	1 (3%)
Musculoskeletal and connective tissue disorders			
Muscular weakness	3 (9%)	3 (9%)	0

Other significant Grade 3 TRAEs: Immune pancreatitis (1), Intestinal perforation (1), Adrenal insufficiency (1), Tubulointerstitial nephritis (1).

Safety Summary
(03/10/2023 Datacut)

ONC-392/BNT316 was tolerated at a dose regimen of 10 mg/kg x 2 then 6 mg/kg, q3w.

- Longest dosing up to 19 cycles and continuing.

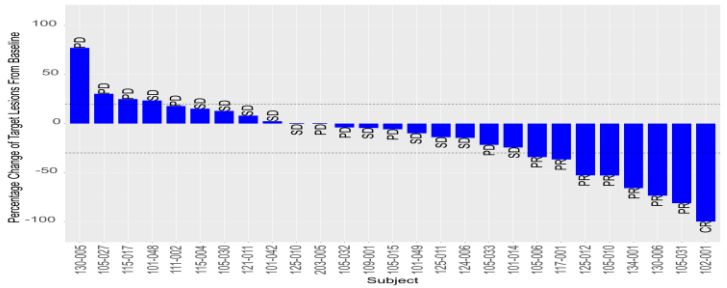
Grade 3–4 TRAEs were observed in 13 pts (39%) with a follow up period from 7 to 18 months. 10 pts (30%) had Gr 3–4 irAEs. No ONC-392/BNT316 related Gr. 5 AE was observed. Significant irAEs include:

- 2 Immune-mediated colitis
- 1 Intestinal perforation
- 1 Gr. 4 ALT/AST increased and immune hepatitis
- 1 Adrenal insufficiency
- 1 Tubulointerstitial nephritis

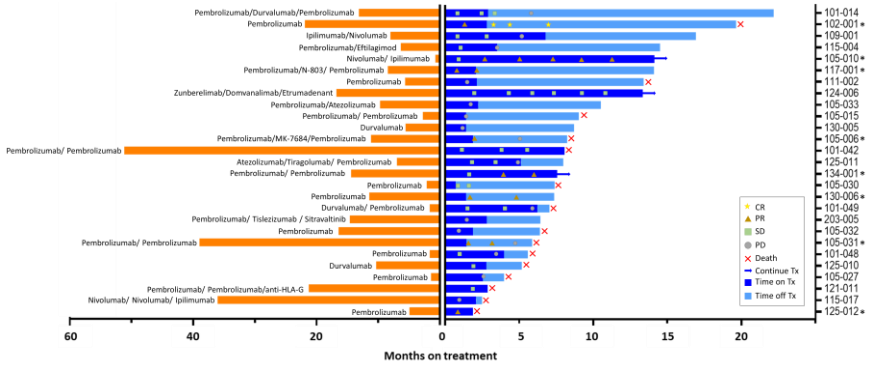
Clinical Activity

Clinical Activity in PD-(L)1 Resistant NSCLC

Target Lesion Best Overall Response (N=27 Evaluable)
ONC-392, 10 mg/kg x 2, then 6 mg/kg, q3w
(101-014 and 102-001: 10 mg/kg x 4, q3w)



Prior Anti-PD-1/PD-L1/CTLA-4 Treatment and ONC-392/BNT316 Treatment



All 27 evaluable patients had prior platinum-based chemotherapy. The * indicates responders to ONC-392 monotherapy.

Clinical Activity

Response rate among the evaluable patients is 29.6% (22.2% confirmed and 7.4% unconfirmed)

- 1 CR and 1 SD in 2 patients with ONC-392/BNT316, 10mg/kg q3w for 4 doses.
- 7 PR and 10 SD among 25 evaluable patients in the expansion cohort with ONC-392 dose regimen of 10 mg/kg x 2, then 6 mg/kg q3w.
- Responders include those that failed multiple IO agents targeting PD-(L)1, CTLA-4, and TIGIT.
- All but 1 responders have been on treatment of PD-(L) 1 targeting agents for >12 weeks, which is provisionally defined as PD-(L)1-resistant NSCLC.

Survival follow up is ongoing

Conclusions

- ONC-392/BNT316 was generally safe and tolerated at 10 mg/kg x2, followed by 6 mg/kg Q3W. Treatment-related AEs are manageable.
- Severe irAE rate in dose expansion cohorts (30%) is considered lower than what was reported for drugs of the similar class.
- Early readout of the expansion cohort shows strong clinical activity in patients with IO-resistant NSCLC.
- These results support initiation of a pivotal study using ONC-392/BNT316 monotherapy for PD-(L)1-resistant NSCLC (Poster TPS#9146, NCT05671510).

BIONTECH

First Phase 3 Study planned: BNT316 (ONC-392) in IO R/R NSCLC[1]

PRESERVE-003 (NCT05671510) – Randomized, open-label, active controlled, multi-center Phase 3 trial

Inclusion criteria

- ≥ 18 years stage IV, metastatic NSCLC
- Prior PD-(L)1 +/- platinum-based chemotherapy
- Prior IO-IO allowed
- ECOG Performance Status: 0 or 1
- Have RECIST 1.1 measurable lesions

Key endpoints

- **Primary:** OS
- Secondary: ORR, PFS, Safety

Stage I (dose-confirmation stage): Assess efficacy and safety of two BNT316 (ONC-392) dosing regimens in comparison to docetaxel

R 1:1:1 N=120

- BNT316 (ONC-392) 6mg/kg with 2 loading doses of 10mg/kg, Q3W (N=40)
- BNT316 (ONC-392) 3mg/kg, Q3W (N=40)
- Docetaxel 75 mg/kg, Q3W (N=40)

- Historic efficacy of docetaxel monotherapy (Garon et al. Lancet. 2014):
  ORR ~10%; mPFS = 3 months; mOS = 9 months

Stage II: Assess safety and efficacy of BNT316 (ONC-392) at the selected dosing regimen versus docetaxel

R 1:1 N=480

- BNT316 (ONC-392) (N=240) TBD: mg/kg, Q3W
- Docetaxel 75 mg/kg, Q3W (N=240)

Trial in Progress

2023 ASCO ANNUAL MEETING

PRESERVE-003 study, Abstract # TPS9146, Poster Time: June 4, 8:00 AM-11:00 AM GMT, Poster #130b

1. Partnered with OncoC4..
PD-1 =Programmed cell death protein 1; IO = immuno-oncology; NSCLC = Non-small cell lung cancer; R/R = Relapsed/Refractory; Q3W = Every three weeks; OS = Overall survival; ORR = Objective response rate; PFS = Progression free survival; ECOG = Eastern Cooperative Oncology Group.

BIONTECH

BNT323 (DB-1303)

Safety and efficacy of DB-1303 in patients with advanced/metastatic solid tumors: A multicenter, open-label, first-in-human, phase 1/2a study.

FIH Phase 1/2 to Evaluate Safety and Tolerability of BNT323 (DB-1303) in Patients with Advanced HER2+ Solid Tumors[1]

Phase 1/2a study design (NCT05150691), multicenter, non-randomized, open-label, multiple-dose, FIH study

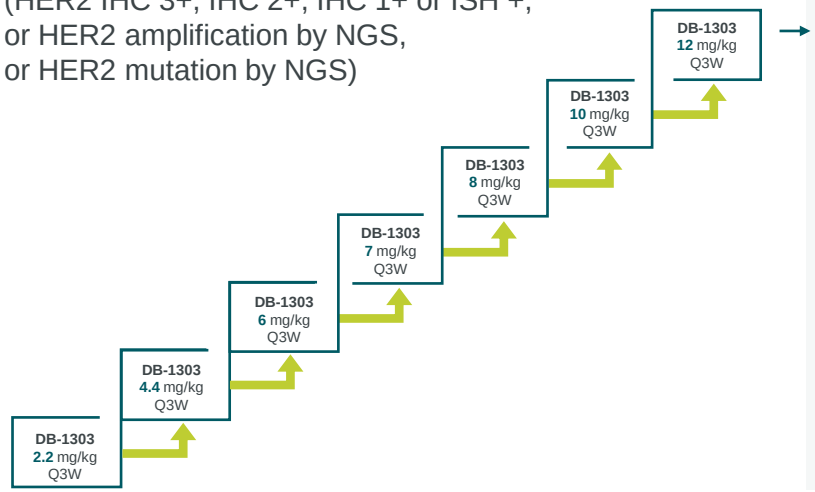
Hamilton E. et al. TiP #9504. Presented at AACR 2023

Inclusion criteria

- Pretreated advanced or metastatic solid tumors
- Histologically confirmed HER2-positive or HER2-expressing cancers
- Previous systemic therapies
- ECOG 0-1
- Adequate organ function

Part 1: **Dose Escalation (n=88 patients)**

(HER2 IHC 3+, IHC 2+, IHC 1+ or ISH +, or HER2 amplification by NGS, or HER2 mutation by NGS)



Part 2a: **Dose expansion (n=165 patients)**

3 weeks DLT window

Indications

- HER2+ gastric, esophageal or gastroesophageal junction adenocarcinoma, CRC
- HR+/HER2-low breast cancer
- HER2+ breast cancer
- HER2 overexpression and HER2-low endometrial cancer
- HER2-mutated NSCLC

Disease progression, withdrawal of consent, unacceptable toxicity

FPI: Jan 2022

Objective: To assess safety, tolerability, pharmacokinetic, preliminary anti-tumor activity at the selected MTD/RP2D

1. Partnered with DualityBio.

IHC = immunohistochemistry; FIH = First in human; Q3W = every three weeks; DLT = dose limiting toxicity; HER2 = human epidermal growth factor 2; HR = hormone receptor; CRC = colorectal cancer; NSCLC = non-small cell lung cancer; MTD = maximum tolerated dose; RP2D = recommended phase 2 dose; ECOG = Eastern Cooperative Oncology Group; FPI = First patient in; LPO = Last patient out; ISH = in-situ hybridization; NGS = next-generation sequencing.

BIONTECH

DB-1303/BNT323: Patient Characteristics and Safety

Baseline and characteristics

	Total (n = 85)
Age, median (range)	52.0 (30.0-79.0)
Female, n (%)	78 (91.8%)
Region, n (%)	
US/AUS	30 (35.3%)
CHN	55 (64.7%)
ECOG PS, n (%)	
0	20 (23.5%)
1	61 (71.8%)
Number of prior systemic regimes in the metastatic disease, median (range)	7.0 (1-27)
Cancer types, n (%)	
Esophageal cancer	2 (2.4%)
Colorectal cancer	3 (3.5%)
HER 2 low breast cancer	21 (24.7%)
Endometrial carcinoma	6 (7.1%)
Ovarian cancer	3 (3.6%)
HER2 positive breast cancer	42 (49.4%)
Vaginal	1 (1.2%)
Gastroesophageal junction adenocarcinoma	1 (1.2%)
Gastic cancer	1 (1.2%)
Non-small cell lung cancer	1 (1.2%)
Sit of metastasis, n (%)	
Brain	18 (21.2%)
Lungs	43 (50.6%)
Liver	34 (40.0%)
HER" IHC results, n (%)	
1+	8 (9.4%)
2+	29 (34.1%)
ISH Positive	10 (11.8%)
ISH Negative or NE	18 (21.2%)
3+	40 (47.1%)
Prior anti-HER2 ADC therapy, n (%)	28 (32.9%)
Prior anti-HER2 antibody therapy, n (%)	47 (55.3%)
Prior anti-HER2 TKI therapy, n (%)	35 (41.2%)
SOD in target lesion, median (n, range)	55.0 (81, 10.5-206.0)

Summary of overall safety

	2.2 mg/kg (n = 1)	4.4 mg/kg (n = 5)	6.0 mg/kg (n = 15)	7.0 mg/kg (n = 29)	8.0 mg/kg (n = 32)	10.0 mg/kg (n = 3)	Total (n = 85)
Any TEAEs	1 (100.0%)	5 (100.0%)	14 (93.3%)	26 (89.7%)	26 (81.2%)	2 (66.7%)	74 (87.1%)
Associated with treatment withdrawal	0	0	0	1 (3.4%)	0	0	1 (1.2%)
Associated with treatment dose reduction	0	0	0	2 (6.9%)	1 (3.1%)	0	3 (3.5%)
Associated with treatment dose interruption	0	0	4 (26.7%)	8 (27.6%)	5 (15.6%)	0	17 (20.0%)
Grade ≥3	0	3 (60.0%)	3 (20.0%)	9 (31.0%)	2 (6.2%)	1 (33.3%)	18 (21.2%)
Serious AEs	0	3 (60.0%)	4 (26.7%)	4 (13.8%)	2 (6.2%)	0	13 (15.3%)
Treatment-related TEAEs	1 (100.0%)	3 (60.0%)	12 (80.0%)	26 (89.7%)	25 (78.1%)	2 (66.7%)	69 (81.2%)
Grade ≥3	0	1 (20.0%)	2 (13.3%)	6 (20.7%)	1 (3.1%)	1 (33.3%)	11 (12.9%)
Serious AEs	0	0	2 (13.3%)	0	0	0	2 (2.4%)

DB-1303 was well tolerated and all AEs were manageable so far

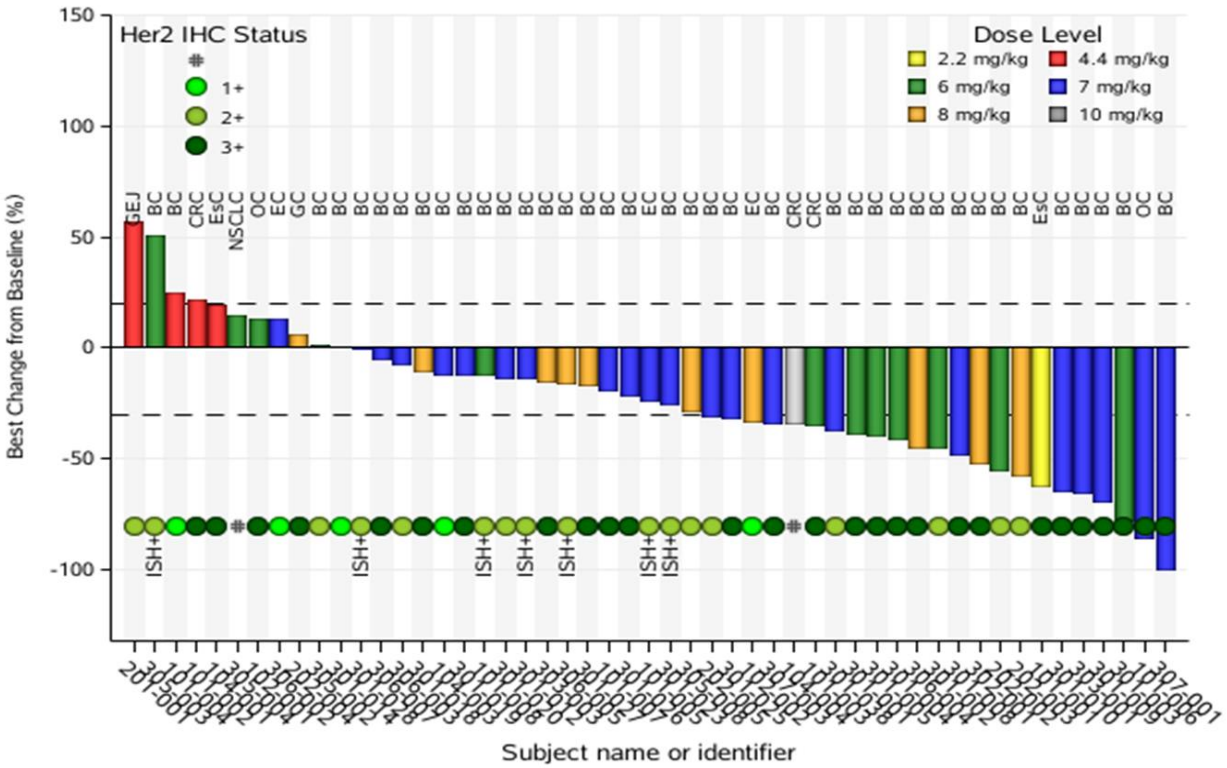
- No DLT was observed in 6 dose levels during dose escalation
- No TEAEs associated with death occurred
- Interstitial lung disease occurred in 2 patients (2.4%, grade 1), without any ≥grade 2
- Few patients experienced neutropenia (10 [11.8]; grade ≥3 in 1 [1.2%] patients,) and alopecia (3 [3.5%], grade 1)

The median duration of treatment was 63.0 (range, 21-211) days, and the median duration of follow-up was 77.0 (range, 7-350) days

BIONTECH

DB-1303/BNT323: Clinical activity

Best overall response for all patients with post-baseline scans



Summary

At the data cutoff (January 13, 2023), 85 patients received DB-1303/BNT316 at 6 dose levels (2.2, 4.4, 6.0, 7.0, 8.0, and 10.0 mg/kg). Here we report the results from dose-escalation

- A total of 68 patients (80.0%) remained on treatment

The unconfirmed **ORR was 44.2% (23/52) and DCR was 88.5% (46/52)** per RECIST v1.1 in heavily pretreated patients with 7 prior systemic regimens including HER2 ADCs. Among patients with post-baseline tumor scan (n = 52) data showed:

- Encouraging activity of DB-1303 was observed in HER2 expressing breast cancer (BC)
  - **HER2 positive BC**: ORR, 50% (13/26); DCR, 96.2% (25/26); **with brain metastases**: ORR, 55.6% (5/9); DCR, 100.0% (9/9)
  - **HER2 low BC**: ORR, 38.5% (5/13), DCR, 84.6% (11/13)
- Antitumor activity of DB-1303 was also observed in non-BC tumor types: ORR, **CRC** (66.7% [2/3]), **EsC** (50.0% [1/2]), **OC** (50.0% [1/2]), and **EC** (33.3% [1/3])

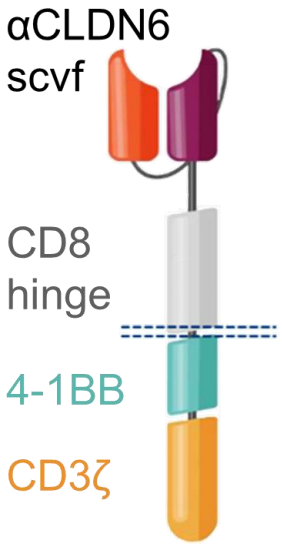
Preliminary antitumor activities were observed in the heavily pretreated HER2 expression patients

3 BNT211

CLDN6 CAR-T cell therapy of relapsed/refractory solid tumors ± a CLDN6-encoding mRNA vaccine: Dose escalation data from the BNT211-01 phase 1 trial using an automated product.

BNT211: first-in-class approach for CLDN6+ solid tumors

CLDN6 CAR T



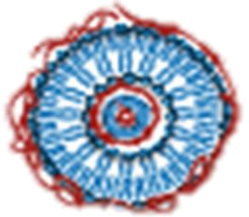
- ✓ Highly sensitive and specific 2nd-generation CAR against CLDN6
- ✓ CLDN6 is absent from healthy adult tissue, but expressed in a variety of cancers[1]

±

CLDN6 CARVac

- ✓ Clinically proven RNA-lipoplex vaccine for body-wide delivery of antigens to dendritic cells[1,2]
- ✓ Amplification and persistence of CAR-T cells by repeat administration[3]

Full-length CLDN6 RNA



Liposomes

BNT211-01: Phase I/IIa, FIH, open-label, multicenter, dose escalation trial

Primary endpoints:
Safety and tolerability, DLTs

Secondary endpoints:
Immunogenicity, ORR, DCR, DoR

Dosing:
- Escalating doses of CLDN6 CAR-T cells ± CLDN6 CARVac (50 µg then 100 µg, if tolerated)
- Lymphodepletion prior to CAR-T cell infusion on Day 1 (DLTs assessed for 28 days)
- CLDN6 CARVac fixed dose (from Day 4) Q3W × 5, then Q6W. CAR-T cell redosing is permitted

Assessments: Efficacy assessments Q6W (RECIST v1.1)

Aim of current analysis
Determine the safety and preliminary efficacy of the automated BNT211 product

R/R advanced CLDN6^{+} solid tumors

Key inclusion criteria

- ≥50% tumor cells with 2+/3+ CLDN6 positivity
- Measurable disease or elevated tumor marker
  ECOG PS 0–1

Phase I dose escalation (manual product): Completed ✓

Monotherapy

DL1 n=3
1×10^{7} CAR T

DL2 n=6
1×10^{8} CAR T

Combination*

DL1 n=4
+ fixed CARVac

DL2 n=9
+ fixed CARVac

* Crossover is possible from monotherapy to combination

Phase I dose escalation with an (automated product): Ongoing

Monotherapy

DL0 n=2
1×10^{6} CAR T

DL1 n=4
1×10^{7} CAR T

DL2 n=4
1×10^{8} CAR T

DL3 n=0
2-5×10^{8} CAR T

Combination

DL1 n=3
+ fixed CARVac

DL2 n=4
+ fixed CARVac

DL3 n=0
+ fixed CARVac

BNT211-01: Safety

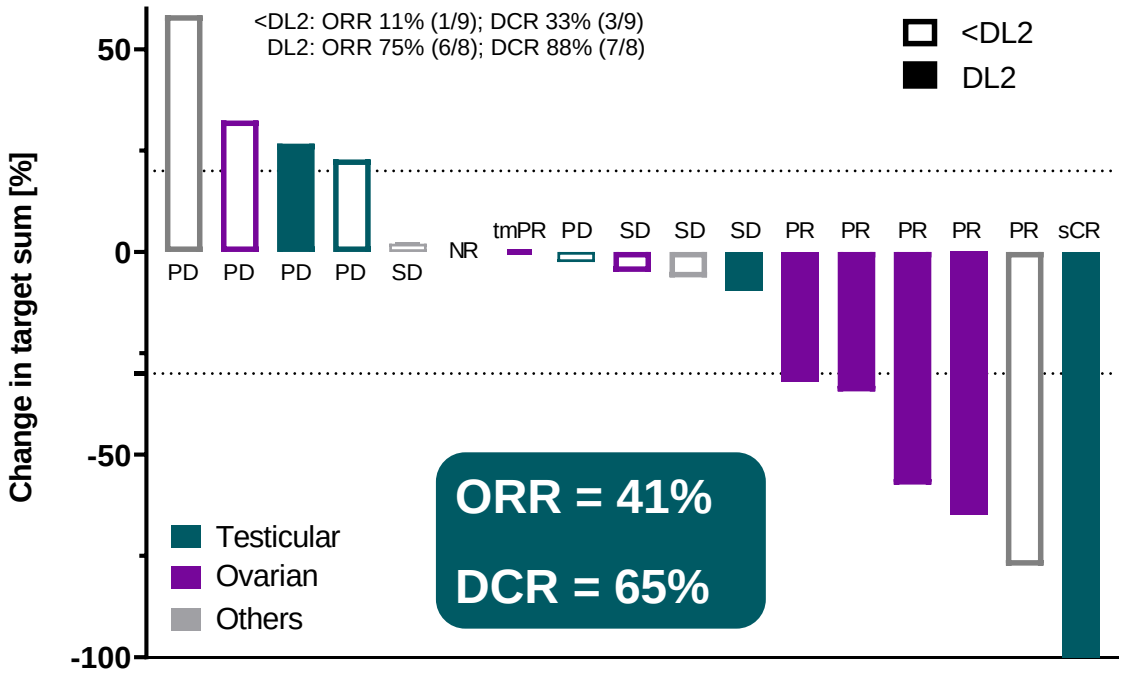
Patients, n	Cohort					
	DL0, Part 1 (N=2) [1]	DL1, Part 1 (N=4)	DL2, Part 1 (N=6)	DL1, Part 2 (N=3)	DL2, Part 2 (N=4)	Total (N=19)
DLTs	0	0	0	0	0	0
Grade ≥3 TEAEs	2 [2]	4	6	2	4	18
Grade ≥3 TEAEs related to IMPs	1	1	5	1	2	10
Related TESAE	1 [3]	0	0	0	0	0
CRS	1 [4]	0	3	1	0	5
Deaths	1 [5]	3	1	0	0	5

Data cutoff: 10 MAR 2023. [1] Both patients crossed over to combination treatment; [2] CTCAE Gr. 3 events were mostly associated with lymphodepletion or elevations of transaminases and bilirubin; [3] 1 patient treated at DL0 experienced sepsis (CTCAE Gr. 3) and subsequently developed Klebsiella infection (CTCAE Gr. 3) and a second sepsis event (Gr. 3); [4] CRS events were all Gr. 1/2, except for 1 transient Gr. 3 event related to CLDN6 CAR-T(A) treatment; [5] Deaths were all due to disease progression.

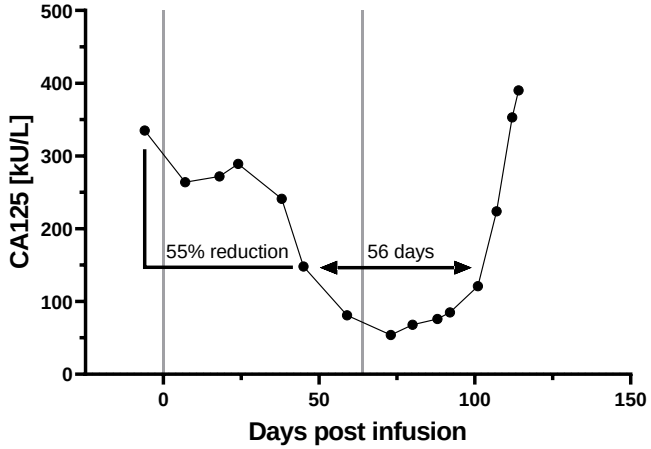
CLDN6 CAR-T (A) cells ± CLDN6 CARVac were well tolerated at evaluated dose levels (no DLTs reported), with a clinical safety profile in line with that of manually produced CLDN6 CAR-T cells

BNT211-01: Efficacy

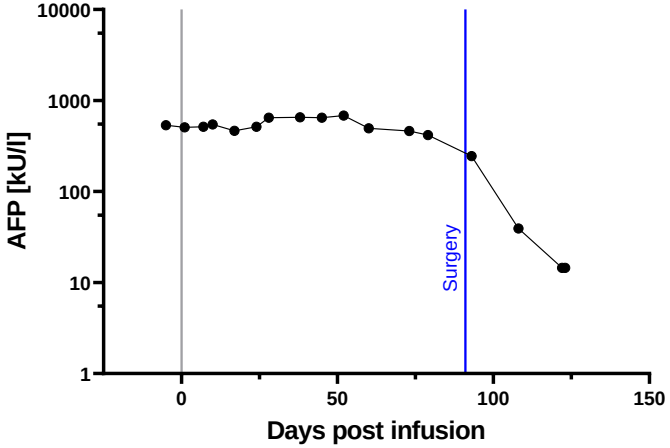
Change in target sum (best response) after CLDN6 CAR-T(A) ± CLDN6 CARVac administration



Tumor marker response (tmPR)



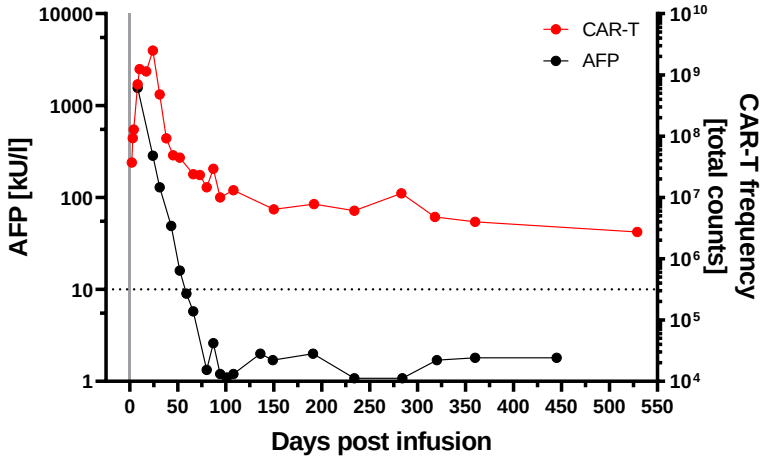
Surgical complete response (sCR)



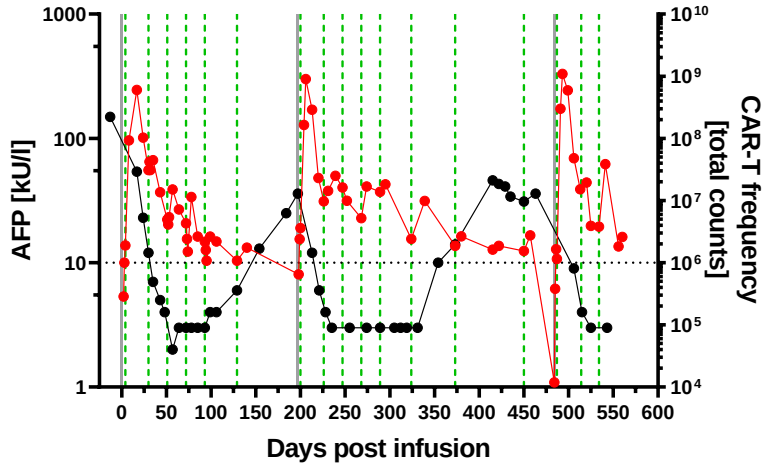
Data cutoff: 10 MAR 2023. Waterfall plot showing best percent change from baseline in sum of target lesion diameters for patients treated with CLDN6 CAR-T(A) ± CLDN6 RNA-LPX. One patient died prior to first assessment (BOR = PD) and one patient had non-measurable disease per RECIST (BOR = SD). Additionally, no response data was available for one patient at the data cutoff (N = 12). Dotted lines show standard response evaluation criteria in solid tumors (RECIST) borders for response assessment (CR = -100%, PR = 30 to -100%, SD = -30 to 20%, and PD = 20% or higher).

BNT211-01: Long-term survivors – Testicular germ cell tumor patients

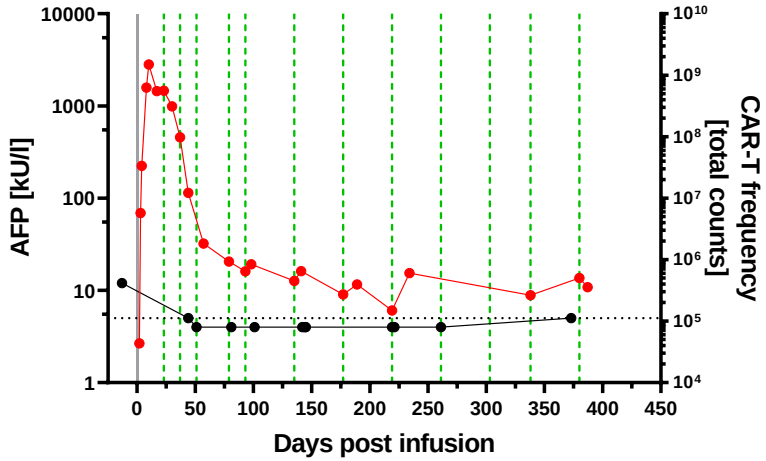
DL2: Ongoing CR (D530)



DL1+CARVac: 3rd PR (D571)



DL2+CARVac: Ongoing SD (D417)



Three of 13 treated germ cell tumor patients (from the manual product cohort) show ongoing clinical benefit

Data cutoff: 10 MAR 2023. BioNTech Data on file.
AFP = alpha fetoprotein; CARVac = CAR T-cell amplifying RNA vaccine; CR = complete response; DL = dose level; PR = partial response; SD = stable disease.

Key take away messages

- **Safety:** CLDN6 CAR-T (A) cells ± CLDN6 CARVac has a moderate safety profile in line with that of manually produced CLDN6 CAR-T cells.
- **Efficacy:** Encouraging signs of activity, with dose-dependent expansion of CAR-T cells translating into ORR of 41% with 7 responses in 17 evaluable patients (ORR 75% at DL2).
- **Outlook:** Follow-up on treated patients and further recruitment to DL2 and DL3 is ongoing. After determination of RP2D for CLDN6 CAR-T (A) cells, a pivotal trial in GCT will be initiated (PRIME designation).