302P

Phase 2 study of the efficacy and safety of BNT327/PM8002 plus systemic chemotherapy as first-line therapy for extensive-stage small-cell lung cancer (ES-SCLC)

Trial registration: NCT05844150; https://clinicaltrials.gov/study/NCT05844150

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CONCLUSIONS

- Efficacy and safety of BNT327 combined with platinum-based chemotherapy were analysed in patients with ES-SCLC, who have not received prior systemic treatment for ES-SCLC:
  - BNT327 combined with platinum-based chemotherapy as a 1L treatment for ES-SCLC demonstrated encouraging efficacy
  - BNT327 in combination with platinum-based chemotherapy exhibited an acceptable tolerability profile, with a low discontinuation rate and no treatment-related deaths reported
- The data presented in this poster support the global Phase 3 trial (NCT06712355) underway in 1L ES-SCLC, part of an extensive clinical program to develop BNT327 in SCLC and NSCLC

Acknowledgements: The authors would like to thank the patients and their families, investigators, co-investigators, and the trial teams at each of the participating institution. This trial was sponsored by Biotheus Inc, a member of the BioNTech Group. BNT327 is fully owned and developed by BioNTech. Medical writing support was provided by Kordula Heinen of BioNTech SE.

Disclosures: Dr Cheng has no financial relationships to disclose beyond Biotheus' support for this trial.

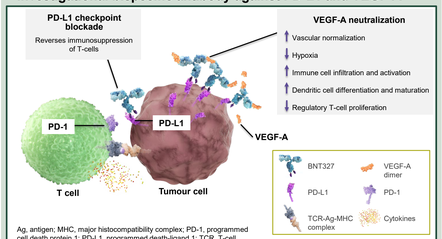
References: 1. Rudin CM, et al. Nat Rev Dis Primers. 2021;7(1):3. 2. Horn L, et al. N Engl J Med. 2018;379(23):2220-2229. 3. Liu SV, et al. J Clin Oncol. 2021;39(6):619-630. 4. Mansfield AS, et al. Ann Oncol. 2020;31(2):310-317. 5. Paz-Ares L, et al. Lancet. 2019;394(10212):1929-1939.

Abbreviations: Ag, antigen; AUC, area under the curve; CR, complete response; CTFI, chemotherapy-free interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern cooperative oncology group performance status; ES, extensive-stage; ICI, immune checkpoint inhibitor; IO, immuno-oncology; irAE, immune-related adverse events; MHC, major histocompatibility complex; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; SAE, serious adverse events; SCLC, small cell lung cancer; SD, stable disease; TCR, T-cell receptor; TEAE, treatment-emergent adverse event; TME, tumour microenvironment; TRAE, treatment-related adverse event; VEGF-A, vascular endothelial growth factor A; 1L first-line; 2L, second-line

Background

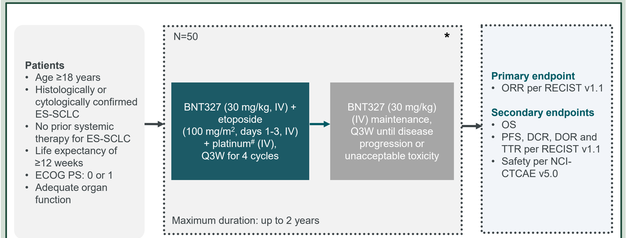
- SCLC accounts for ~15% of lung cancer cases, with an estimated 250,000 new cases globally per year[1]. Despite the recent advances, prognosis remains poor, underscoring a high unmet need for therapies that provide durable clinical benefit[2-5]
- BNT327/PM8002 is an investigational bispecific antibody, targeting both PD-L1 and VEGF-A in the tumour and TME. Binding to PD-L1 overexpressed on tumour cells is designed to restore effector T-cell function and localize VEGF-A neutralization within the TME, reversing the negative impact of VEGF signalling on immune cell infiltration and activation and normalizing tumour vasculature leading to tumour growth inhibition. Dual targeting of PD-L1 and VEGF-A combines two complementary modalities, aiming to improve efficacy and safety (**Figure 1**).
- Here, we report preliminary data from an ongoing Phase 2 trial (**Figure 2**) of BNT327 combined with chemotherapy in first-line ES-SCLC for the first time

Figure 1. Proposed mechanism of action of BNT327, an investigational bispecific antibody against PD-L1 and VEGF-A



Trial design

Figure 2. Trial design of BNT327 in 1L ES-SCLC (NCT05844150) – an open label, single arm, multi-site phase 2 trial



#carboplatin: AUC = 5, total single dose ≤ 750 mg on Day 1 or cisplatin: 75 mg/m² on Day 1
*Tumour assessment every 6 weeks (±5 days) for 48 weeks from first dose and thereafter every 9 weeks (±5 days) until disease progression or receipt of other antitumour therapy

Results: Baseline characteristics

- Enrolment was completed on November 21, 2023, with 50 patients enrolled to the trial. Baseline patient and disease characteristics are presented in **Table 1**

Table 1. Baseline patient and disease characteristics

Characteristic	N=50
Age, median (range), years	59.0 (46-75)
Sex, n (%)	
Male	34 (68.0)
Female	16 (32.0)
ECOG PS, n (%)	
0	10 (20)
1	40 (80)
Metastatic sites, n (%)	
0	0 (0)
1-2	23 (46.0)
≥ 3	27 (54.0)
Metastases, n (%)	
Brain, yes	5 (10.0)
Liver, yes	15 (30.0)
Smoker, n (%)	33 (66)

Results: Efficacy

At the cut-off date of December 20, 2024, 48 patients had completed at least one tumour evaluation, and five patients remained on treatment:

- Median treatment exposure was 5.7 months (95% CI: 4.4, 7.2)
- Median follow-up time was 14.5 months (95% CI: 13.4, 15.3)
- Disease control rate was 97.9% (**Table 2** and **Figure 3**)
- Confirmed ORR was 85.4% and unconfirmed ORR 87.5% (**Table 2**)
- 12-month OS rate was 72.7%. Median OS was not yet mature (**Table 2**)

Table 2. Efficacy endpoints

Endpoint	N=48
Best overall response, n (%)	
PR	42 (87.5)
SD	5 (10.4)
PD	1 (2.1)
Unconfirmed ORR, % (95% CI)	87.5 (74.8, 95.3)
Confirmed ORR, % (95% CI)	85.4 (72.2, 93.9)
DCR, % (95% CI)	97.9 (88.9, 100.0)
Median DOR, months (95% CI)	5.5 (3.75, 6.77)
Median PFS, months (95% CI)	**6.9 (4.34, 8.21)**
6-month PFS rate, % (95% CI)	54.2 (39.2, 67.0)
12-month PFS rate, % (95% CI)	15.1 (6.56, 27.0)
Median OS, months (95% CI)	**16.8 (14.3, --)**
6-month OS rate, % (95% CI)	91.7 (79.3, 96.8)
12-month OS rate, % (95% CI)	72.7 (57.6, 83.1)
OS events, n (%)	17 (35.4)

Figure 3. Change from baseline in tumour size

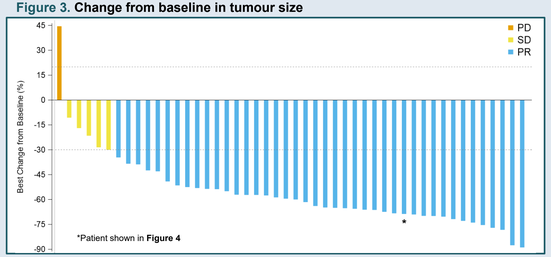


Figure 4. Example of tumour shrinkage observed in one patient treated in the trial

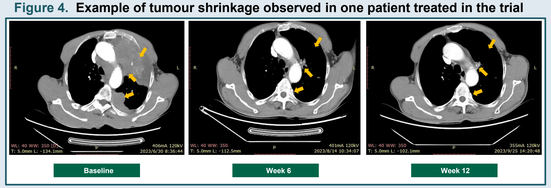


Figure 5. Change from baseline in tumour size

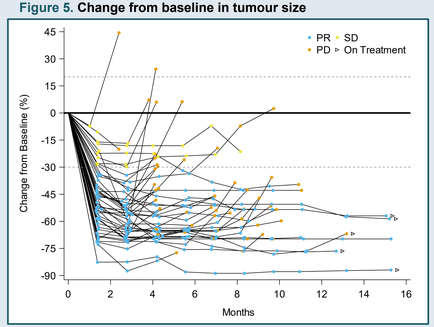
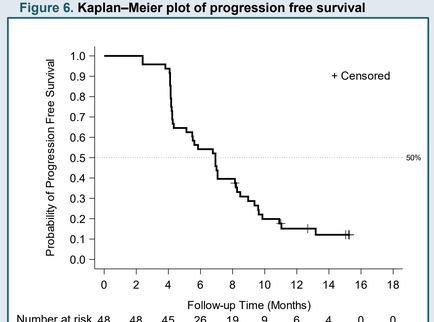


Figure 6. Kaplan–Meier plot of progression free survival



Results: Safety

Fifty patients were included in the safety analysis:

- Safety data (data cut-off: December 20, 2024) are summarized in **Table 3**
- All patients experienced at least one adverse event related to treatment with BNT327 and/or chemotherapy (TRAE), with 43 patients (86%) experiencing Grade 3 or higher TRAEs
- The most commonly observed TRAEs (**Table 4**) were: neutrophil count decrease (90%), anaemia (80%), white blood cell count decrease (76%) and platelet count decrease (62%)
- No treatment-related deaths were reported
- TRAEs of special interest were all Grade 1-3 with no grade 4/5 events, including hypertension, proteinuria, and various forms of haemorrhage (epistaxis, gastric, gingival, and intraventricular), occurring in 26% (Grade 3: 16%), 52% (Grade 3: 14%), 6% (Grade 3: 0%), 2% (Grade 3: 2%), 4% (Grade 3: 0%) and 2% (Grade 3: 0%) of patients, respectively
- Immune-related adverse events occurred in 42% of patients (21/50), with Grade 3 or higher in 10% (5/50). Three patients (6%) discontinued treatment due to TRAEs

Table 3. Safety summary

Patients, n (%)	N=50
TEAE	50 (100)
TRAE#	50 (100)
irAE	21 (42)
Grade ≥3 TEAE	44 (88.0)
Grade ≥3 TRAE#	43 (86.0)
Grade ≥3 irAE	5 (10)
SAE	24 (48.0)
TRSAE#	20 (40.0)
AE leading to:	
Treatment discontinuation	
TEAE	5 (10.0)
TRAE#	3 (6.0)
Dose reduction*	
TEAE	13 (26.0)
TRAE#	13 (26.0)
Death	
TEAE	2 (4.0)
TRAE#	0

#AEs related to BNT327 and/or chemotherapy
*Dose reduction was only allowed for chemotherapy

Table 4. Adverse events related to BNT327 and/or chemotherapy observed in ≥ 20% of the patients

	Grade, n (%)		
TRAE# ≥ 20%; N=50	All	3	4
Neutrophil count decreased	45 (90.0)	19 (38.0)	9 (18.0)
Anaemia	40 (80.0)	10 (20.0)	0
White blood cell count decreased	38 (76.0)	12 (24.0)	1 (2.0)
Platelet count decreased	31 (62.0)	5 (10.0)	7 (14.0)
Proteinuria	26 (52.0)	7 (14.0)	0
Alanine aminotransferase increased	16 (32.0)	2 (4.0)	0
Aspartate aminotransferase increased	15 (30.0)	0	0
Gamma-glutamyltransferase increased	14 (28.0)	2 (4.0)	0
Nausea	14 (28.0)	0	0
Hypertension	13 (26.0)	8 (16.0)	0
Hypercholesterolaemia	12 (24.0)	1 (2.0)	0
Lymphocyte count decreased	10 (20.0)	0	1 (2.0)

Scan to view — **Suppl. Table 1: TRAE ≥ 10%**

BNT327: Clinical trials in lung cancer

- BNT327 is being investigated in a comprehensive clinical development program in lung cancer (**Supplementary Table 2**). Global trials are ongoing in SCLC (1L, Phase 3, NCT06712355) and NSCLC (1L, Phase 2/3, NCT06712316 and 2L, Phase 2, NCT06841055). A Phase 3 trial (NCT06616532) in 2L SCLC is ongoing in China.
- Results from a Phase 2 trial (NCT05879068) in 2L SCLC are reported at ELCC2025 (see poster 332P)

Scan to view — **Supplementary Table 2: Global clinical development program for BNT327 in lung cancer**

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Presented at the European Lung Cancer Congress (ELCC 2025), Paris, France

Updated phase II efficacy and safety results of BNT327/PM8002 combined with paclitaxel as second-line (2L) therapy in small cell lung cancer (SCLC)

332P

Trial registration: NCT05879068; https://clinicaltrials.gov/study/NCT05879068

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CONCLUSIONS

- Efficacy and safety of BNT327 combined with paclitaxel were analysed in patients with SCLC who progressed after 1L platinum-based chemotherapy:
  - BNT327 combined with paclitaxel as a 2L treatment for SCLC demonstrated encouraging efficacy in both IO-naive and IO-treated patients
  - BNT327 in combination with paclitaxel exhibited an acceptable tolerability profile, with a low discontinuation rate and adverse events consistent with those expected from chemotherapy and in line with the expected mode of action of BNT327
- The data presented in this poster further inform the ongoing clinical development of BNT327 in lung cancer. Specifically, they support the Phase III trial (NCT06616532) underway in China, evaluating BNT327 in combination with paclitaxel, as well as a Phase I/II trial of BNT327 with BNT324/DB-1311, a B7H3 ADC (NCT06892548). Both trials investigate 2L treatment of SCLC.

Acknowledgements: The authors would like to thank the patients and their families, investigators, co-investigators, and the trial teams at each of the participating institution. This trial was sponsored by Biotheus Inc, a member of the BioNTech Group. BNT327 is fully owned and developed by BioNTech. Medical writing support was provided by Kordula Heinen of BioNTech SE.

Disclosures: Dr Cheng has no financial relationships to disclose beyond Biotheus' support for this trial.

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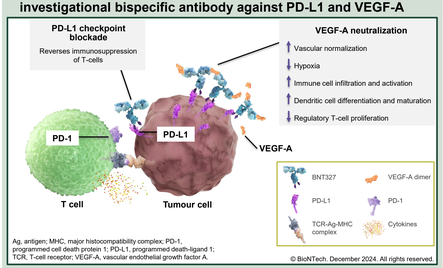
Abbreviations: Ag, antigen; CR, complete response; CTFI, chemotherapy-free interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern cooperative oncology group performance status; IO, immuno-oncology; #AE, immune-related adverse events; MHC, major histocompatibility complex; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; SAE, serious adverse events; SCLC, small cell lung cancer; SD, stable disease; TCR, T-cell receptor; TEAE, treatment-emergent adverse event; TME, tumour microenvironment; TRAE, treatment-related adverse event; VEGF-A, vascular endothelial growth factor A; 1L, first-line; 2L, second-line.

Background

- SCLC is an aggressive cancer characterized by high proliferative rate, high vascularity, and early development of widespread metastases[1-4]. The prognosis for patients who are refractory or relapse after 1L therapy remains poor.[5] There is a high unmet need to improve the poor outcomes for this patient population
- BNT327/PM8002 is an investigational bispecific antibody, targeting both PD-L1 and VEGF-A in the tumour and TME. Binding to PD-L1 overexpressed on tumour cells is designed to restore effector T-cell function and localize VEGF-A neutralization within the TME, reversing the negative impact of VEGF signalling on immune cell infiltration and activation and normalizing tumour vasculature leading to tumour growth inhibition. Dual targeting of PD-L1 and VEGF-A combines two complementary modalities, aiming to improve efficacy and safety (**Figure 1**)

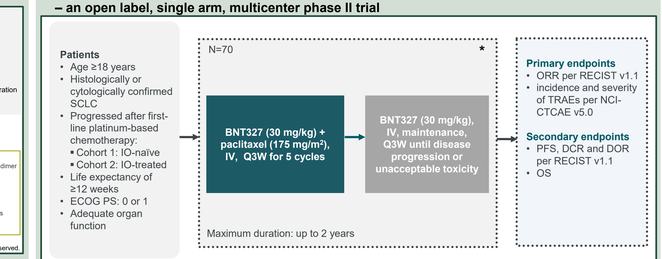
Figure 1. Proposed mechanism of action of BNT327, an investigational bispecific antibody against PD-L1 and VEGF-A



- Here, we report updated data from an ongoing Phase II trial (NCT05879068, **Figure 2**) of BNT327 combined with paclitaxel in 2L SCLC conducted in China. An earlier data cut with fewer patients was previously presented at ESMO 2023 (1992P)

Trial design

Figure 2. Trial design of BNT327 in combination with paclitaxel in 2L SCLC (NCT05879068) – an open label, single arm, multicenter phase II trial



*Tumor assessments were performed every 6 weeks for the first year after the first dose, and then every 12 weeks thereafter until disease progression or additional antineoplastic therapy, whichever occurred first

Results: Baseline characteristics

- Enrolment was completed on 11 Jun 2024, with 70 patients enrolled (26 IO-naïve, 44 IO-treated; 13 chemo-free interval < 30 days).
- Further baseline patient and disease characteristics are presented in **Table 1**

Table 1. Baseline patient and disease characteristics

Characteristic	N=70
Age, median (range), years	62.5 (37-78)
Male | Female, n (%)	57 (81.4) | 13 (18.6)
ECOG PS 0 | 1, n (%)	21 (30) | 49 (70)
Metastatic sites 0 | 1-2 | ≥ 3, n (%)	0 (0) | 41 (58.6) | 29 (41.4)
Metastases, n (%)	
Brain, yes	13 (18.6)
Liver, yes	21 (30.0)
Chemotherapy-free interval, n (%)	
< 30 days	13 (18.6)
< 90 days	35 (50.0)
< 180 days	55 (78.6)

Results: Efficacy

At the cutoff date of December 20, 2024, eight patients remaining on treatment:

- Median treatment exposure was 4.7 months (95% CI 3.7, 5.4); IO-naïve: 4.8 months (95% CI: 2.7, 14.7), IO-treated: 4.3 months (95% CI: 3.6, 5.4) in 65 efficacy evaluable patients
- Median follow-up time was 17.9 months (95% CI: 15.7, 23.1); IO-naïve: 24.4 months (95% CI: 23.1, 26.5), IO-treated: 11.0 months (95% CI: 9.7, 17.4)
- Patients demonstrated encouraging anti-tumour activity regardless of prior IO treatment with an overall disease control rate of 87.7% (**Table 2**, **Figure 3** and **4**)
  - Confirmed ORR was 41.5% and unconfirmed ORR 56.9% (**Table 2**)
- Median overall survival was 14.3 months (95% CI 10.9, 19.9) and median progression-free survival was 5.5 months (95% CI: 4.1, 7.2), with comparable outcomes for IO-naïve and IO-treated patients (**Table 2**)

Figure 3. Change from baseline in tumour size

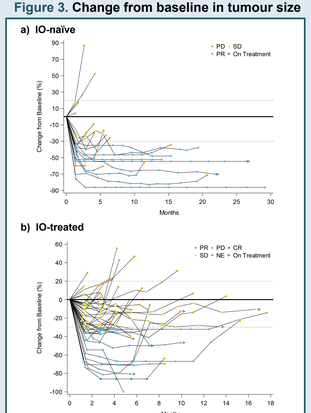


Figure 4. Best overall response for change from baseline in tumour size

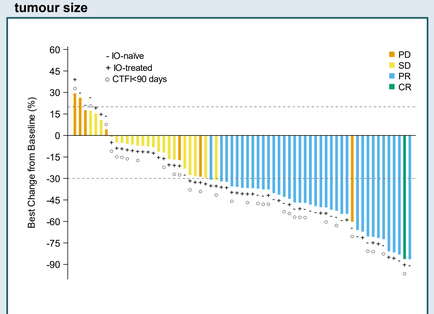


Figure 5. Kaplan–Meier plot of progression free survival

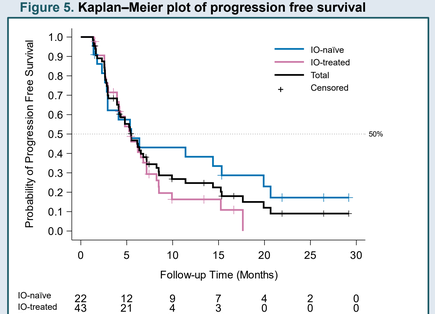


Table 2. Efficacy endpoints

Endpoint	Efficacy evaluable population N=65	IO-naïve N=22	IO-treated N=43
Best change from baseline, n (%)			
CR	1 (1.5)	0 (0)	1 (2.3)
PR	36 (55.4)	16 (72.7)	20 (46.5)
SD	20 (30.8)	2 (9.1)	18 (41.9)
PD	8 (12.3)	4 (18.2)	4 (9.3)
Unconfirmed ORR, % (95% CI)	56.9 (44.0,69.2)	72.7 (49.8, 89.3)	48.8 (33.3, 64.5)
Confirmed ORR, % (95% CI)	41.5 (29.4, 54.4)	50.0 (28.2, 71.8)	37.2 (23.0, 53.3)
DCR, % (95% CI)	87.7 (77.2, 94.5)	81.8 (59.7, 94.8)	90.7 (77.9, 97.4)
Median DOR, months (95% CI)	5.6 (3.3, 10.0)	11.5 (1.6, 19.4)	5.5 (3.0, 7.1)
Median PFS, months (95% CI)	5.5 (4.1, 7.2)	5.5 (2.8,15.3)	5.4 (4.1, 6.8)
6-month PFS rate, % (95% CI)	46.7 (33.9, 58.6)	47.9 (25.9, 66.9)	46.1 (30.3, 60.5)
12-month PFS rate, % (95% CI)	24.7 (14.4, 36.5)	38.3 (18.4, 58.0)	16.3 (6.3, 30.5)
Median OS, months (95% CI)	14.3 (10.9, 19.9)	14.7 (9.5, --)	14.3 (8.5, --)
6-month OS rate, % (95% CI)	83.1 (71.5, 90.3)	86.4 (63.4, 95.4)	81.4 (66.2, 90.2)
12-month OS rate, % (95% CI)	61.2 (47.2, 72.5)	59.1 (36.1, 76.2)	65.5 (48.5, 78.0)
OS events, n (%)	34 (52.3)	14 (63.6)	20 (46.5)

Results: Safety

70 patients were included in the safety analysis:

- Safety data are summarized in **Table 3**: A total of 69 patients (98.6%) experienced at least one adverse event related to treatment with BNT327 and/or chemotherapy (TRAE). Among these, 55 patients (78.6%) experienced Grade 3 or higher TRAEs
- The most commonly observed TRAEs (**Table 4**) were:
  - Neutrophil count decrease (80%)
  - White blood cell count decrease (80%)
  - Anaemia (63%)
  - Platelet count decrease (48.6%)
- Two Grade 5 TRAEs occurred (pneumonitis and immune-mediated hepatitis)
- TRAEs of special interest were generally mild-to-moderate and comprised proteinuria (30%, including 7.1% grade 3), hypertension (8.6%) and various forms of haemorrhage (epistaxis (2.9%), gastrointestinal, gingival bleeding, subcutaneous, and urethral; each 1.4%)
- There were no Grade 4/5 TRAEs of special interest
- Any-grade immune-related adverse events occurred in 23 (32.9%) patients (Grade ≥ 3 in 5 [7.1%])

Table 3. Safety summary

Patients, n (%)	N=70
TEAE	69 (98.6)
TRAE#	69 (98.6)
irAE	23 (32.9)
Grade ≥3 TEAE	58 (82.9)
Grade ≥3 TRAE#	55 (78.6)
Grade ≥3 irAE	5 (7.1)
SAE	35 (50.0)
TRSAE#	29 (41.4)
AE leading to:	
Treatment discontinuation	
TEAE	6 (8.6)
TRAE#	5 (7.1)
Dose reduction*	
TEAE	15 (21.4)
TRAE#	15 (21.4)
Death	
TEAE	7 (10.0)
TRAE#	2 (2.9)

#AEs related to BNT327 and/or chemotherapy
*Dose reduction was only allowed for chemotherapy

Table 4. Adverse events related to BNT327 and/or chemotherapy observed in ≥ 20% of the patients

	Grade, n (%)		
TRAE# ≥ 20%; N=70	All	3	4
Neutrophil count decreased	56 (80.0)	27 (38.6)	18 (25.7)
White blood cell count decreased	56 (80.0)	22 (31.4)	3 (4.3)
Anaemia	44 (62.9)	1 (1.4)	0
Platelet count decreased	34 (48.6)	3 (4.3)	1 (1.4)
Asthenia	21 (30.0)	0	0
Proteinuria	21 (30.0)	5 (7.1)	0
Hypoaesthesia	20 (28.6)	0	0
Weight decreased	19 (27.1)	0	0
Alopecia	15 (21.4)	0	0
Hyperuricaemia	14 (20.0)	0	0

Scan to view

Suppl. Table 1: TRAE ≥ 10%

BNT327: Clinical trials in lung cancer

- BNT327 is being investigated in a comprehensive clinical development program in lung cancer (**Supplementary Table 2**). Global trials are ongoing in SCLC (1L, Phase III, NCT06712355) and NSCLC (1L, Phase II/III, NCT06712316 and 2L, Phase II, NCT06841055). A Phase III trial (NCT06616532) in 2L SCLC is ongoing in China.
- Results from a Phase II trial (NCT05844150) in 1L SCLC are reported at ELCC2025 (see poster 302P).

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Supplementary Table 2: Global clinical development program for BNT327 in lung cancer

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Presented at the European Lung Cancer Congress (ELCC 2025), Paris, France