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Final results of the BGBC008 Phase 2, multicenter study of bemcentinib and pembrolizumab (bem+pembro) in 2nd line (2L) advanced non-squamous (NS) non-small cell lung cancer (NCT03184571)

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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Background

- Treatment options in 2L metastatic NS NSCLC remain limited with modest outcomes to date.
- AXL, a receptor tyrosine kinase, mediates resistance to immune- and chemotherapy (CT) and is a poor prognostic biomarker in NSCLC.
- Bemcentinib (bem), a highly selective oral AXL inhibitor, potentiates the immune-checkpoint inhibitor (ICI) effect in pre-clinical models, providing a strong scientific rationale for the bem+pembro combination in this patient population (PP).

Methods

Phase 2 open label study with bemcentinib + pembrolizumab in 2L NSCLC

Inclusion criteria
NS (adenocarcinoma) histology
PD-L1 All comers
Stage IV

Regimen
Pembrolizumab 200mg fixed dose q 3 weeks up to 2 years
Bemcentinib 400mg loading, 200mg QD

Primary endpoint
Objective Response Rate

Secondary endpoints
DoR, DCR, PFS, mOS
Survival at 12 months
Safety

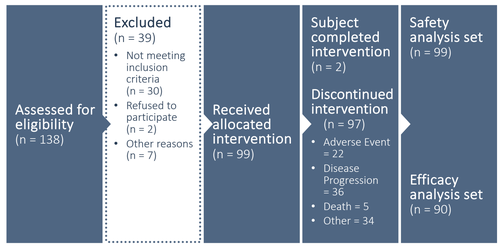
Exploratory endpoints
Response by Biomarker expression

Cohort A (n=44)
Prior 1L platinum chemotherapy treatment
- 2nd line metastatic NS NSCLC

Cohort B (n=27)
Prior 1L anti-PD-1/L1 treatment
- Disease control on 1L for ≥12 wks. before progression
- 2nd or 3rd line metastatic NS NSCLC

Cohort C (n=19)
Prior 1L anti-PD-1/L1 + platinum-chemo treatment
- Disease control on 1L for ≥12 wks. before progression
- 2nd or 3rd line metastatic NS NSCLC

Consort Diagram and Patient Demographics (n=99)



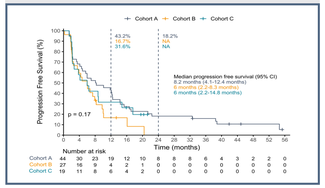
Age	Median	65
	Range	39-86
ECOG at screening	0	46
	1	53
Sex	Female	34
	Male	65
Smoking status	Ex-smoker	90
	Never smoked	72
	Current smoker	15

Topline Efficacy Results

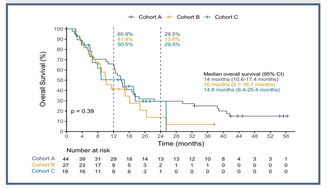
Parameter	Cohort A n = 44	Cohort B n = 27	Cohort C n = 19	Total n = 90
ORR, n% (90% CI)	22.7 (12.9, 35.5)	0 (0, 10.5)	0 (0, 14.6)	11.1 (6.2, 18.1)
PR, n% (confirmed)	22.7	-	-	11.1
DCR, n% (95% CI)	54.5 (38.8, 69.6)	44.4 (25.5, 64.7)	52.6 (28.9, 75.6)	51.1 (40.3, 61.8)
mDOR, mo (95% CI)	8.1 (3.9, 25.6)	-	-	8.1 (3.9, 25.6)
mPFS, mo (95% CI)	8.2 (4.1, 12.4)	6 (2.2, 8.3)	6 (2.2, 14.8)	6.2 (4.4, 8.7)
mOS, mo (95% CI)	14 (10.6, 17.4)	10 (6.7, 16.1)	14.8 (6.4, NA)	13 (10, 15.3)

mPFS and mOS by cohort

mPFS by cohort

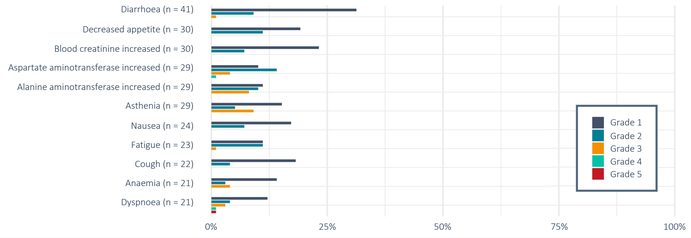


mOS by cohort



Data cut-off: DBL 23.12.2022 (Q4 2022)

TEAEs affecting ≥ 20% of patients (Grades 1 to 5)



Exploratory Efficacy Results

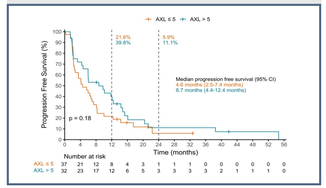
	AXL expression ≤5 n = 37	AXL expression >5 n = 32	PD-L1 high (TPS ≥50%) n = 12	PD-L1 low (TPS 1-49%) n = 25	PD-L1 negative (TPS <1%) n = 31
mPFS (months)	4.6	8.7	5.3	6	7
mOS (months)	9.9	14.8	11.2	10.6	12.4

AXL expression cut-point is based on the H-score, a weighted IHC staining intensity score calculated as (1* percent cells with low expression)+ (2 * percent cells with medium expression) + (3* percent cells with high expression).

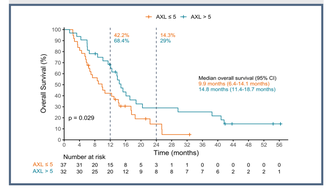
PD-L1 was measured by IHC (22C3 assay)

AXL status impacts mPFS and mOS

mPFS by AXL status



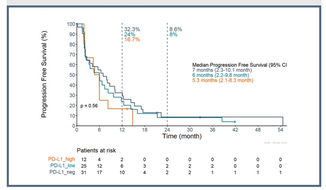
mOS by AXL status



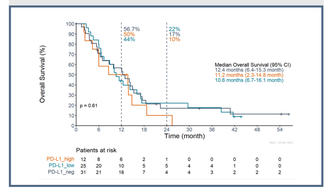
Data cut-off: DBL 23.12.2022 (Q4 2022)

Clinical benefit regardless of PD-L1 status

Median progression free survival



Median overall survival



TPSPD-L1 negative <1%;PD-L1 low = 1-49%
PD-L1 high ≥50%

Conclusions

The combination of bem+pembro demonstrated promising anti-tumor activity with longer mPFS and mOS than previously reported in previously treated advanced adenocarcinoma of the lung.

The safety of the combination is manageable with the majority of TRAEs reported in this study mild (Grade 1, 27%) or moderate (Grade 2, 23%)

AXL expression by IHC >5 was associated with higher ORR, longer PFS and OS.

Clinical benefit was observed regardless of the PD-L1 status, supporting the scientific hypothesis of bemcentinib's role in potentiating the effect of immune-checkpoint inhibitors.

The findings support further investigation of this combination therapy as a potential treatment option for NSCLC patients who have progressed after prior therapy.

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