Safety and efficacy of OR502, an antibody targeting leukocyte immunoglobulin-like receptor B2 (LILRB2), ± cemiplimab in patients with advanced solid tumors from a phase 1 study

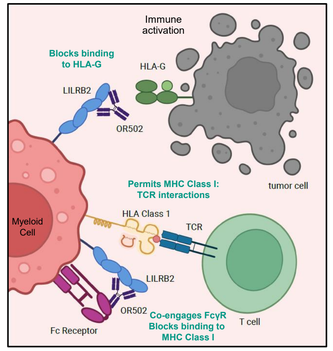
Poster 171
Abst. 2524

Sen S[1], Vandross A[2], Sommerhalder D[3], Salkeni M[4], Puri K[5], Sarapa N[6], Bouchlaka MN[5], Skingley L[6], Cronier D[6], Yefimenko M[6], Bexon A[6].

OR502 – best in class LILRB2 antibody

- OR502 is a humanized IgG1 antibody that blocks LILRB2 binding to HLA-class 1 ligands[1]
- Preclinical evidence demonstrates that OR502:
  - Rescues T cell effector functions by reducing and preventing new and existing TAMs developing immunosuppressive phenotypes
  - Amplifies anti-PD-1 activity[1]
  - Reprograms myeloid cells through FcγR co-engagement[1]
  - Is effective in a human xenograft melanoma murine model[1]

Fig 1: OR502 mode of action



- Thus, OR502 + CPI is a rational approach for targeting immunosuppression and enhancing T cell responses in the TME (Fig. 1)
- Here we report on the completed OR502 ± cemiplimab dose escalation cohorts from this ongoing, phase 1-2 FIH study (NCT06090266)

Study design

- Thirty-nine subjects with advanced solid cancers
- ≥ 1 prior systemic SOC anti-cancer therapy, or could not tolerate, refused, or no suitable SOC option was available
- IV OR502 100–1600 mg Q3W ± cemiplimab 350 mg

For full study design, see Poster 315b

Table 1: Demographics and clinical characteristics

Parameter	OR502 (n=19)	OR502 + cemiplimab (n=20)
Median age, years (range)	62 (47–82)	64 (23–85)
Female (%)	63	50
ECOG PS = 1 (%)	79	80
Median prior systemic regimens (range)	3 (0–11)	3 (0–7)
Most common tumor types (%)		
Sarcoma	37	25
NSCLC	21	15
Colon or CRC	0	20

Table 2: Study objectives

Primary	Evaluate safety, tolerability and identify dose for further development
Secondary	Characterize PK, immunogenicity and anti-tumor activity
Exploratory	Evaluate effect on tumor microenvironment Assess association between pharmacodynamic markers and tumor responses

Contact: alice.bexon@bexonclinical.com

Results

OR502 ± cemiplimab is well tolerated

- No DLTs, treatment-related deaths, SAEs or grade ≥ 3 TRAEs (Table 3)
- No significant findings in vital signs, ECG or laboratory safety test results
- One discontinuation (400 mg OR502) due to CTCAE grade 2 pneumonitis with grade 2 hypothyroidism
- OR502 infusions were extended from 30 to 60 minutes
- Secondary prophylaxis (acetaminophen, diphenhydramine) implemented after IRR

Table 3: Related AEs in ≥ 10% subjects

	OR502 (n=19)		OR502 + cemiplimab (n=20)	
CTCAE Grade	**1–2 n (%)**	**≥ 3 n (%)**	**1–2 n (%)**	**≥ 3 n (%)**
Any related TEAE	10 (52.6)	0	6 (30)	0
Fatigue	3 (15.8)	0	0	0
IRR	3 (15.8)	0	2 (10)	0
Nausea	3 (15.8)	0	0	0

OR502 ± cemiplimab early anti-tumor efficacy

- Thirty-five subjects (90%) evaluable for RECIST 1.1 assessment (Table 4)
- Durable SD: sarcomas, CSCC, thymoma, thyroid carcinoma, melanoma, HCC, CRC
- PK roughly dose-proportional (Fig. 7); RO near-complete ≥ 200 mg (Fig. 8); RO and PK not affected by cemiplimab
- Thirteen deaths due to PD

Table 4: Best objective response

Response	OR502 (n=17)	OR502 + cemiplimab (n=18)
PR/cPR	2/1 (Fig. 2 & 3)	1/1 (Fig. 4)
SD	9	8
Durable SD ≥ week 12	7	4
ORR %	12	6
DCR: (CR + PR+ SD) %	65	50

Fig 2. cPR: male, 62 yrs, melanoma, prior pembro & ipi/nivo

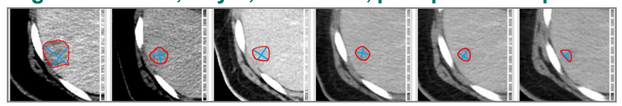


Fig 3: PR in female, 76 yrs, NSCLC prior chemo & durva

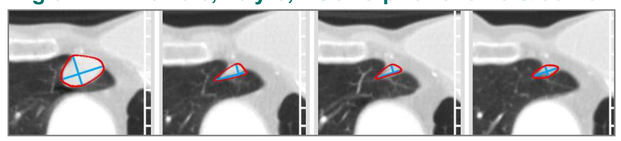


Fig 4: cPR in male, 61 yrs, soft tissue sarcoma, no prior Tx

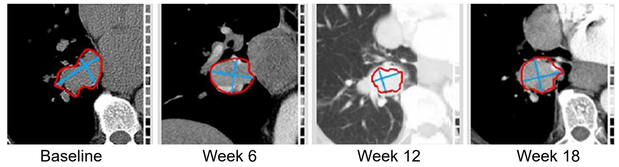


Fig 5: Over 1 in 4 patients had ≥ 12 weeks treatment

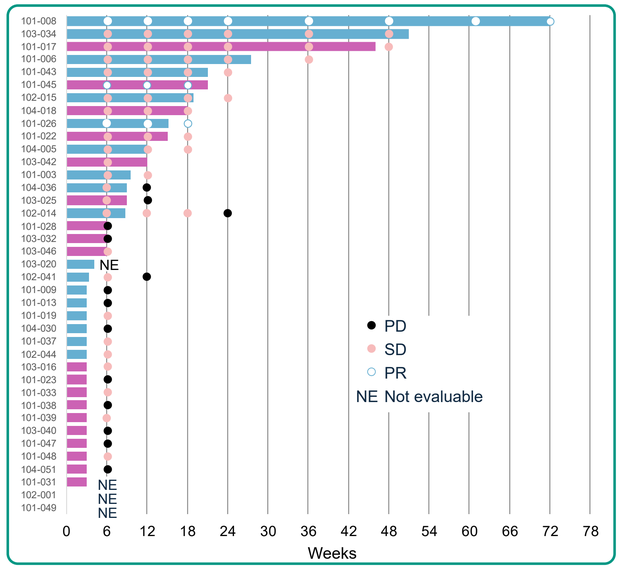


Fig 6. Promising tumor growth control at 12 weeks

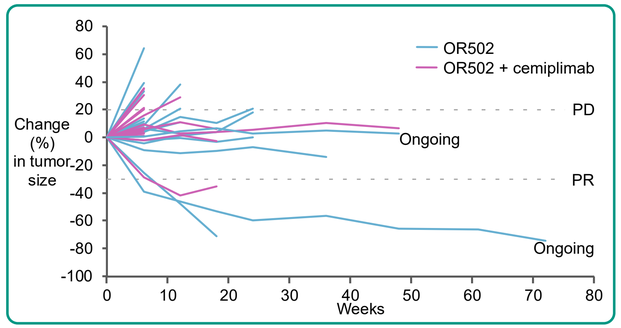


Fig 7: OR502 achieved pharmacologically active serum exposures within dose range tested

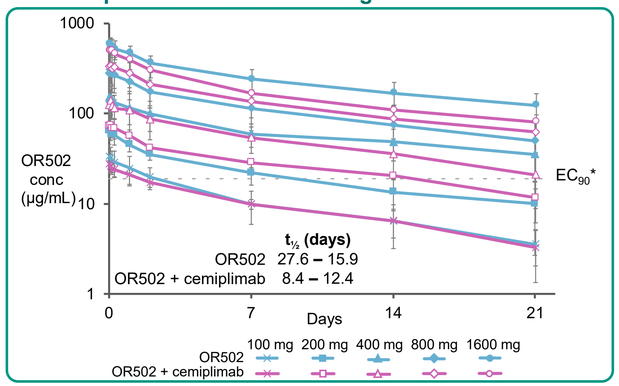
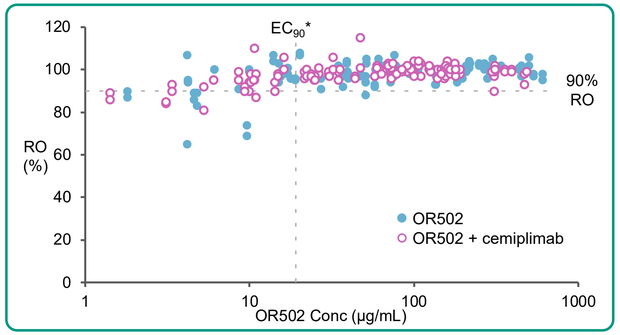


Fig 8. PK and RO support OR502 800 mg dose



★ Concentration to achieve 90% maximal biological activity based on in vitro pharmacology studies.

Conclusions

- OR502 has excellent safety and tolerability as monotherapy and in combination with cemiplimab
- OR502 800 mg chosen as RP2D based on efficacy, PK and RO
- Two mini-expansion cohorts are recruiting to evaluate OR502 800 mg Q3W ± cemiplimab in subjects with cutaneous melanoma or NSCLC

Study OR502-101 has been approved by the Salus non-profit Institutional Review Board in Austin, TX. Study OR502-101 is registered as NCT06090266 in www.clinicaltrials.gov **Acknowledgements:** Study OR502-101 is conducted with support from the Cancer Prevention Research Institute of Texas (CPRIT) DP230076. OncoResponse is grateful to the subjects who participated in this study, whose time and dedication is invaluable for the development of OR502 as potential new treatment for advanced cancer. **Author affiliations** 1. NEXT Oncology, Dallas, TX, USA. 2. NEXT Oncology, Austin, TX, USA. 3. NEXT Oncology, San Antonio, TX, USA. 4. NEXT Oncology, Fairfax, VA, USA. 5. OncoResponse, Inc., Seattle, WA, USA. 6. Bexon Clinical Consulting, Montclair, NJ, USA. **References:** 1. Bouchlaka M, et al. J Immunother Cancer. 2023; 11(Suppl 1): A556. **Abbreviations:** AE: adverse event. CPI: checkpoint inhibitor. cPR: confirmed partial response. CR: complete response. CRC: colorectal cancer. CSCC: cutaneous squamous cell carcinoma. CTCAE: Common Terminology Criteria for Adverse Events. DCR: disease control rate. DLT: dose-limiting toxicity. Durva: durvalumab. ECG: electrocardiogram. ECOG: Eastern Cooperative Oncology Group. FIH: first-in-human. HCC: hepatocellular cancer. HLA: human leukocyte antigen. Ig: immunoglobulin. ipi/nivo: ipilimumab/nivolumab. IRR: infusion-related reaction. LILRB2: leukocyte immunoglobulin-like receptor B2. MHC: major histocompatibility complex. NSCLC: non-small cell lung cancer. ORR: overall response rate. PD: progressive disease / pharmacodynamics. PD-1: programmed cell death protein 1. Pembro: pembrolizumab. PK: pharmacokinetics. PR: partial response. Q3W: every 3 weeks. RECIST: Response Evaluation Criteria in Solid Tumors. RO: receptor occupancy. RP2D: recommended phase 2 dose. SAE: serious adverse event. SD: stable disease. SOC: standard of care. $T_{1/2}$: half-life. TCR: T cell receptor. TME: tumor microenvironment. TEAE: treatment emergent adverse event. TRAE: treatment-related adverse event. Tx: treatment.