Abstract 1047P

Lung-MAP S1800A—Exploratory analysis of prior immunotherapy outcomes on OS with ramucirumab plus pembrolizumab for NSCLC with PD on prior ICI

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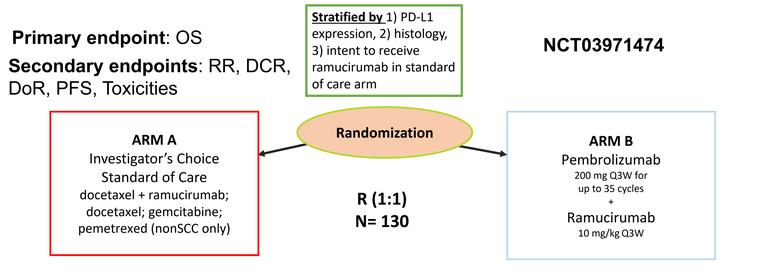
BACKGROUND

- Frontline therapy for advanced NSCLC includes PD-1/L1 inhibition in most patients without activating mutations.
- Although survival has improved with these therapies, resistance develops that requires additional therapy for most patients.
- Acquired resistance to immune checkpoint inhibitor therapy is a major area of unmet need for patients with NSCLC.
- Developing therapies to overcome resistance will become increasingly important as immunotherapy is incorporated across all stages of NSCLC.
- VEGF is important in modulating the tumor immune microenvironment by induction of PD-L1 expression on dendritic cells and suppresses maturation; impeding T cell extravasation; inhibition of proliferation and cytotoxicity of cytotoxic T lymphocytes; stimulating the proliferation of T regulatory (Treg) cells; and mediating effects on myeloid-derived suppressor cells (MDSCs).
- VEGFR2 inhibition decreases infiltration of suppressive immune cells while increasing mature dendritic cells.
- Combination blockade of PD1 (pembrolizumab) and VEGFR2 (ramucirumab) may overcome resistance by reducing tumor neovascularization with upregulation of proinflammatory cytokines.
- Vascular endothelial growth factor receptor (VEGFR) and ICI therapy has demonstrated benefit across multiple solid tumor types.
- S1800A demonstrated improved overall survival with pembrolizumab and ramucirumab compared to standard-of-care following progression on prior platinum-based doublet and ICI in patients with advanced NSCLC (HR: 0.69 [80% CI, 0.51-0.92]; 1-sided p-value=0.05).

SCHEMA

Phase II randomized study of ramucirumab plus pembrolizumab versus standard of care for advanced non-small cell lung cancer previously treated with immunotherapy—Lung-MAP non-matched sub-study S1800A



Key eligibility: 1) Previously received both PD-1 or PD-L1 inhibitor therapy and platinum-based doublet chemotherapy either sequentially or combined, with PD on at least 84 days after initiation of ICI and platinum-based doublet therapy; 2) ECOG 0-1; 3) all patients met eligibility to receive ramucirumab

RESULTS

Table 1. Prior Immunotherapy and Chemotherapy Received

	Chemotherapy followed by Immunotherapy# (n=59)	Combination Immunotherapy and Chemotherapy (n=74)	TOTAL* (n=136)
RANDOMIZED TREATMENT			
Ramucirumab + Pembrolizumab	36	32	69
Standard of Care (Inv. Choice)	23	42	67
HISTOLOGY			
Adenocarcinoma	26	47	75
Squamous Cell Carcinoma	32	23	55
Mixed < 50% squamous cell carcinoma	0	1	1
Mixed >= 50% squamous cell carcinoma	0	0	1
Other non-small cell, NOS	1	3	4
PRIOR IMMUNOTHERAPY RECEIVED			
Pembrolizumab	13	66	82
Nivolumab	27	0	27
Durvalumab	18	5	23
Atezolizumab	1	3	4
ADDITIONAL TREATMENT ORDER			
Chemotherapy received prior to Combination Immunotherapy and Chemotherapy	n/a	50	50
Chemotherapy received after Immunotherapy	12	11	23
STAGE WHEN CHEMOTHERAPY FIRST RECEIVED			
Stage I-III	34	17	52
Stage IV	25	57	84
BEST RESPONSE ON PRIOR IMMUNOTHERAPY			
Partial Response	17	31	48
Stable Disease	30	34	66
Progression**	12	8	21
Unknown	0	1	1
TIME ON PRIOR IMMUNOTHERAPY			
Median (Range)	8.3 (2.8, 56.8)	7.8 (0, 43.7)	8.0 (0, 56.8)
< 6 Months	18	22	41
6 - < 12 Months	23	36	59
12+ Months	18	16	36
TIME BETWEEN PRIOR IMMUNOTHERAPY AND RANDOMIZATION			
Median (Range)	2.6 (0.7, 21.4)	2.4 (0.7, 16.3)	2.5 (0.7, 21.4)
< 6 Months***	43	62	105
6 - < 12 Months	4	7	13
12+ Months	12	5	18

*Total to include all patients, except three who received Immunotherapy followed by Chemotherapy not described separately.
#Most patients were enrolled without the requirement of immediate past therapy as immunotherapy.
**For those whose best response on prior IO was progression (n=21), the median time between start of therapy until progression was 4.9 months (range: 3.0-14.7, IQR: 3.8-7.1).
***There were four patients who received 84 days or less of prior IO. One patient received one cycle and stopped due to side effects. One patient received for 42 days and stopped IO (reason unknown) but continued with chemo for another year. Two patients received IO for exactly 84 days.

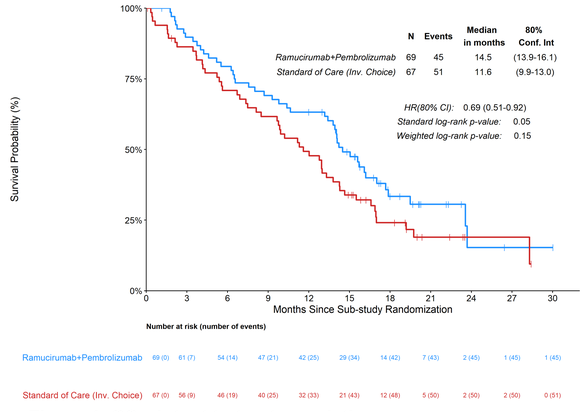


Figure 1. OS—intent to treat population

Figure 2. OS by best response to prior immunotherapy, prior response—A) Partial response; B) Stable disease; C) Progressive disease

Median follow up: 17.9 months

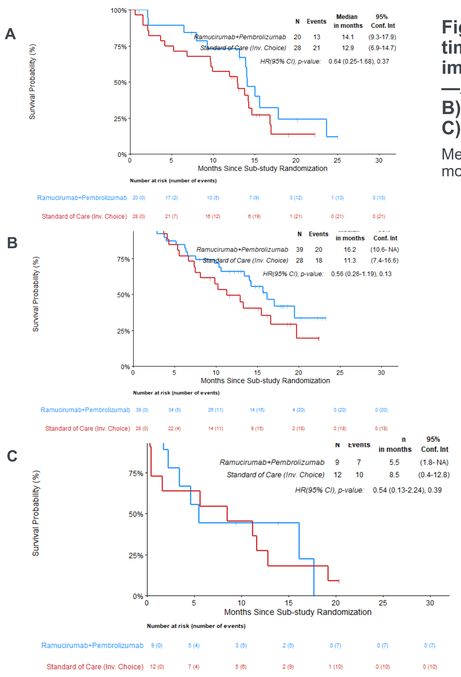


Figure 3. OS by time on prior immunotherapy—A) ≥12 months; B) 6-12 months; C) <6 months

Median follow up: 17.9 months

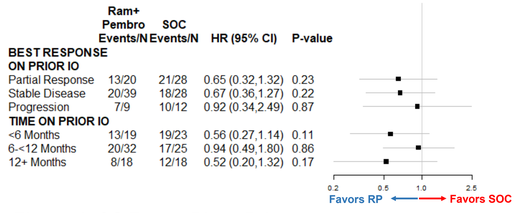


Figure 4. OS Forest Plot—Prior response to immunotherapy and time on prior immunotherapy

CONCLUSIONS

- Treatment with ramucirumab and pembrolizumab significantly increased OS compared to SOC in advanced NSCLC following progression on prior ICI.
- In this exploratory analysis, prior partial response and stable disease to previous ICI suggests a biological benefit from the combination in patients who develop acquired resistance to ICI.
- Prior time on ICI less than 6 months and more than 12 months showed greater benefit with ramucirumab and pembrolizumab.
- A larger randomized trial is required to confirm these findings.

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DECLARATION OF INTERESTS

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