Pembrolizumab re-challenge in patients with relapsed non-small cell lung cancer (NSCLC): a preliminary report of the REPLAY phase II trial - cohort I

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BACKGROUND

Current front-line treatment for NSCLC includes PD1/PDL1 checkpoint inhibitors (CPI) alone or in combination with chemotherapy.

Second line treatment approach is an unmet need, mainly limited to Docetaxel, and the utility of CPI is an open question. Here we report preliminary data of cohort 1 of the REPLAY trial that assess the efficacy of pembrolizumab re-challenge.

METHODS

REPLAY is an open label phase II multicenter exploratory study.

For cohort 1 eligible patients had confirmed NCSLC (PDL1 ≥ 1%) who progressed after a line of treatment containing a CPI with documented benefit (SD, PR, CR) for at least 16 w treatment and/or progression within 12 w after last dose of CPI.

Post CPI progression patients must have received then, previously to be enrolled, at least four courses of chemotherapy without progression. ECOG 0-1, adequate organ function and no G3-4 IrAEs were allowed.

Patients received pembrolizumab 200 mg iv q3w until disease progression or toxicity up to 2 y. Primary endpoint was to evaluate ORR (RECIST 1.1), and secondary objectives included PFS, OS, safety and biomarker discovery.

Table 1 Patients characteristics

Patients (n)	55 (100%)	
Sex	Male	40 (72.7%)
	Female	15 (27.3%)
Age		63.7
Ethnicity	Caucasian	53 (96.4%)
Performance Status	0	15 (27.3%)
	1	39 (70.9%)
Smoking Status	Former	39 (70.9%)
	Current	8 (14.5%)
	Never	7 (12.7%)

Patients (n)	55 (100%)	
Histology	Non-Squamous	36 (65.5%)
	Squamous	19 (34.5%)
Stage	IIIA-IIIB	4 (7.2%)
	IV	51 (92.8%)
Prior treatment	3rd line	12 (21.8%)
	4th line	20 (36.4%)
	≥ 5th line	23 (41.8%)

FIGURE 1 Cohort I Schema

Table 2 Overall Response Rate

Evaluable patients	**54 (100.0%)**
Complete Response	0 (0.0%)
Partial Response	1 (1.9%)
Stable Disease	21 (38.9%)
Progression Disease	26 (48.1%)
Unknown	6 (11.1%)
End of treatment due to	
Disease Progression	47 (85.5%)
Principal Investigator's decision	1 (1.8%)
Death	6 (10.9%)

Table 3 Toxicity profile (CTCAE v5.0)

	Patients	Grade				
	N	1	2	3	4	5
Any adverse event	28 (50.9%)	14	11	3	0	0
Diarrhea	7 (12.7%)	6	1	0	0	0
Nausea	3 (5.5%)	2	1	0	0	0
Fatigue	8 (14.5%)	3	5	0	0	0
Fever	1 (1.8%)	1	0	0	0	0
Pain	1 (1.8%)	0	1	0	0	0
Alanine aminotransferase increased	2 (3.6%)	1	1	0	0	0
Alkaline phosphatase increased	2 (3.6%)	1	0	1	0	0
Aspartate aminotransferase increased	1 (1.8%)	1	0	0	0	0
Blood bilirubin increased	1 (1.8%)	0	0	1	0	0
Creatinine increased	1 (1.8%)	1	0	0	0	0
GGT increased	1 (1.8%)	0	1	0	0	0
Anorexia	2 (3.6%)	2	0	0	0	0
Hypokalemia	1 (1.8%)	0	1	0	0	0
Hypomagnesemia	2 (3.6%)	2	0	0	0	0
Hypophosphatemia	1 (1.8%)	0	0	1	0	0
Arthralgia	3 (5.5%)	1	2	0	0	0
Pruritus	6 (10.9%)	3	3	0	0	0

RESULTS

55 patients were treated, including male 40 pts (72.7%), with median age 63.7 y, ECOG I (70.9%) and non squamous histology 33 pts (60%). Forty-three pts (78.2%) had received > 3 treatment lines. An objective partial response was observed in 1 patient (1.9%) and stable disease observed in 21 pts (38.9%).

Median number of pembrolizumab cycles were 5,3. 28 pts (50.9%) developed TRAEs: 14 pts (25.5%) G1, 11 pts (20%) G2 and 3 pts (5.5%) G3. Most frequent AEs were fatigue (14.5%), diarrhea (12.7%), pruritus (10.9%) and arthralgia (5.5%).

No treatment-related deaths were reported. With a median follow-up of 7.6 m (0.3-27 m) median PFS was 1.6 m (IC95% 1.3 – 1.9 m), PFS at 6 m 23.6% and 7.3% at 12 m. OS was 8.3 m (IC95% 5.1 - 11.5 m), OS at 6 m 59.1% and at 12 m 35.2%.

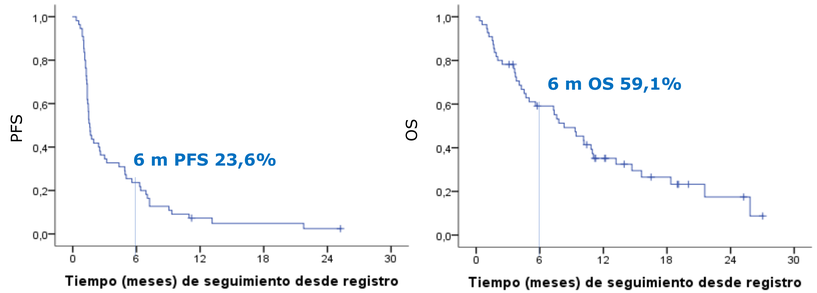

FIGURE 2 Progression Free Survival 1.6 m (1.3-1.9 m) ; Overall Survival 8.3 m (5.1m – 11.5 m)

CONCLUSION

Pembrolizumab re-challenge is a feasible and well tolerated strategy with non-overwhelming but definitive activity in a relevant proportion of patients (one PR, 24% PFS at 6 months) in this late treatment line setting.

A comprehensive predictive biomarker program is ongoing.

GECP lung cancer research

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