Preliminary data on first line combination carboplatin, taxane and pembrolizumab therapy followed by maintenance pembrolizumab for cytoreduced ovarian cancer with residual disease.

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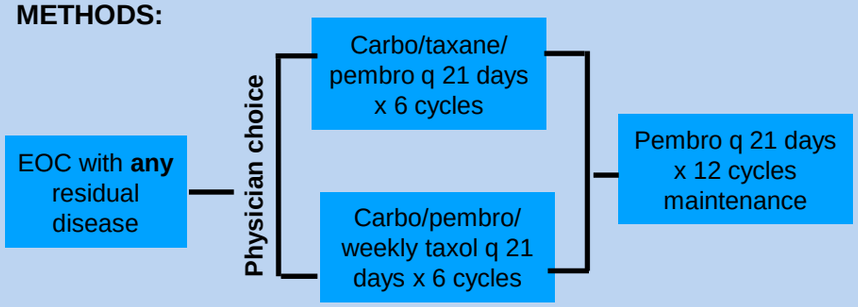
BACKGROUND:

Ovarian cancer is the leading cause of mortality from gynecologic malignancies. Stage of disease and extent of residual disease are the most important prognostic factors. The greatest difference in long term outcomes have been observed between patients with optimal microscopic disease (no visible residual) compared with optimal macroscopic or suboptimal. Pembrolizumab is a highly selective humanized monoclonal antibody that blocks the interaction between programmed death (PD-1) and its ligand, PD-L1 and PD-L2; it has shown single agent activity in heavily pretreated PD-L1 positive ovarian cancer patients. Data is very limited on the safety and efficacy of carboplatin + taxane + pembrolizumab. With the support of Merck pharmaceuticals we began a multi-institutional investigator initiated phase II trial to determine the safety and efficacy of first line combination therapy with carboplatin/ taxane/ pembrolizumab followed by pembrolizumab maintenance therapy in advanced EOC patients with any residual disease after cytoreductive surgery. This represents our preliminary data on 10 of the planned 30 participants.

METHODS:



RESULTS:

Ten patients have been enrolled to date. 3 patients had undergone suboptimal debulking with > 1cm residual disease and 7 had macrosocpic residual < 1cm. Chemotherapy regimens given are listed in Table 2. The most common grade 3/4 toxicity noted has been neutropenia (70%), see Table 3. Pneumonitis has been the only immune related toxicity to date and required trial discontinuation in that participant.

RESULTS:

Table 1. Patient Baseline Characteristics

	Subjects (N)
Age (Median)	67 years
Histology	
Serous	6
Clear Cell	2
Carcinosarcoma	2
Stage	
III	7
IV	3
Cytoreductive Surgery Residual	
Macroscopic optimal	7
Suboptimal (> 1 cm)	3

Table 2. Treatment Regimens

	Subjects (N)	# Cycles
Pembro + Carboplatin q 21 days /Weekly Paclitaxel	8	39
Pembro + Carboplatin/ Taxane q21 days	2	12
Pembrolizumab Maintenance	5	30

Table 3. Combination Treatment Adverse Events

	N (%) Grade 3/4	N (%) Any Grade
Hematologic		
Anemia	4 (40)	8 (80)
Neutropenia	7 (70)	8 (80)
Gastrointestinal	0	9 (90)
Metabolic	2 (20)	8 (80)
Respiratory	1 (10)	8 (80)
Genitourinary	1 (10)	3 (30)
Nervous System	1 (10)	8 (80)
Cardiac	1 (10)	1 (10)

Table 4. Combination Treatment Immune Related AEs *

	N (%) of subjects	Grade
Pneumonitis	1 (10)	4

***No immune related AEs on maintenance to date**

RESULTS (continued):

Five patients have completed combination therapy and are on maintenance, 1 has completed all maintenance therapy. PFS censored at progression or last follow-up is listed in Table 5. Three patients have progressed to date (Table 5). One progressed while on combination therapy and 2 while on maintenance therapy.

Table 5. Outcomes

	Residual Disease	Clinical Status	Months from surgery
1	Macroscopic optimal	NED	9
2	Suboptimal	PD	8
3	Macroscopic optimal	WD	—-
4	Suboptimal	PD	14
5	Suboptimal	NED	13
6	Macroscopic optimal	PD	6
7	Macroscopic optimal	NED	7
8	Macroscopic optimal	NED	6
9	Macroscopic optimal	NED	6
10	Macroscopic optimal	NED	3

NED, no evidence of disease; PD, progression of disease; WD, withdrawn (pneumonitis)

CONCLUSIONS:

- Combination carboplatin/ taxane/ pembrolizumab therapy has manageable safety and toxicity profile.
- Efficacy is still under evaluation.

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