## 291 PHASE IB STUDY OF SELICRELUMAB (CD40 AGONIST) IN COMBINATION WITH ATEZOLIZUMAB (ANTI-PD-L1) IN PATIENTS WITH ADVANCED SOLID TUMORS

[1]Fabrice Barlesi*, [2]Martijn Lolkema, [3]Kristoffer Staal Rohrberg, [4]Cinta Hierro, [5]Aurelien Marabelle, [6]Albiruni Abdul Razak, [7]Luis Teixeira, [8]Valentina Boni, [9]Wilson H Miller, [10]Charu Aggarwal, [11]Martin Stern, [12]Olivera Cirovic, [12]Olivera Cirovic, [12]Barbara Romagnoli, [12]Randolph Christen, [13]Raksha Dodia, [13]Kevin Smart, [12]Bernhard Reis, [11]Nicolas Staedler, [14]Carl Watson, [15]Neeltje Steeghs. *[1]Gustave Roussy Cancer Campus, Villejuif, France; [2]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [3]Rigshospitalet, Copenhagen, Denmark; [4]Vall d'Hebron University Hospital, Barcelona, Spain; [5]Gustave Roussy, Université Paris Saclay, Villejuif, France; [6]Princess Margaret Cancer Centre, Toronto, Canada; [7]Saint-Louis Hospital, APHP, Paris, France; [8]START Madrid, Madrid, Spain; [9]Jewish General Hospital, Montreal, Canada; [10]University of Pennsylvania, Philadelphia, USA; [11]Roche Innovation Center Zurich, Schlieren, Switzerland; [12]Roche Innovation Center Basel, Basel, Switzerland; [13]Roche Innovation Center Welwyn, Welwyn Garden City, UK; [14]A4P Consulting Ltd, Sandwich, UK; [15]Netherlands Cancer Institute, Amsterdam, Netherlands*

**Background** Selicrelumab is a human IgG2 agonistic anti-CD40 monoclonal antibody. Binding of the antibody to CD40 expressed on antigen-presenting cells results in T- cell priming and T-cell dependent anti-tumor activity. In response to T-cell activation, tumor cells express programmed-death ligand 1 (PD-L1) that can suppress effector T-cells. Atezolizumab interrupts this feedback loop by blocking PD-L1, thereby supporting the combination with selicrelumab.

**Methods** This phase Ib open-label, multicenter, dose escalation (DE)/expansion clinical study (NCT02304393) investigated safety, pharmacokinetic (PK), pharmacodynamics (PD) and efficacy of selicrelumab in combination with atezolizumab in unselected patients with advanced/metastatic solid tumors, not amenable to standard therapy. In DE cohorts, a single dose of selicrelumab was given, either by intravenous (IV) infusion at a 16 mg fixed dose or subcutaneously (SC) at a range from 1 to 64 mg/dose. In dose-expansion cohorts (small bowel and colorectal cancer, head and neck squamous cell carcinoma [HNSCC] and non-small cell lung carcinoma), patients received multiple doses of selicrelumab SC at a dose of 16 mg. In all treatment cohorts, patients received atezolizumab at a fixed dose of 1200 mg IV Q3W.

**Results** In this study, 140 patients were treated. This included 95 patients in DE cohorts (6 patients in the IV cohort, 89 patients in the SC cohorts) and 45 patients in dose-expansion cohorts. In the IV cohort, infusion related reaction was the most frequent treatment-related adverse event (TRAE; 50%), while Grade $\geq$ 3 TRAE occurred in 1 patient (16.7%). In this cohort one dose-limiting toxicity (DLT) was reported (Grade 3 pancytopenia). In the SC cohorts, the most frequent TRAE was injection site reaction (ISR; 92%). Four DLTs were reported in four patients: three Grade 3 ISR and one Grade 3 transaminase increase. Grade $\geq$ 3 TRAE were reported in 22 patients (16.4%). Anti-tumor activity was observed across cohorts receiving SC selicrelumab (dose range 1 to 36 mg). Eight of 80 evaluable patients in DE cohorts experienced objective responses (9% ORR). In the dose-expansion HNSCC cohort, three of 16 evaluable patients responded (15.8% ORR). There were no objective responses in the IV cohort. Treatment with selicrelumab resulted in significant peripheral B-cell depletion and activation and CD8+ T cell proliferation.

**Conclusions** Treatment with selicrelumab in combination with atezolizumab was well tolerated in patients with advanced solid tumors. Signals of clinical and PD activity were observed. However, efficacy of the combination in this unselected population was limited, when compared to monotherapy efficacy of atezolizumab.

**Trial Registration** NCT02304393

**Ethics Approval** This study was approved by the local IRB at each participating study site.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0291

## 292 IMMUNE CHECKPOINT INHIBITOR INDUCED OVERLAPPING CARDIAC AND NEUROMUSCULAR TOXICITIES: HIGHLIGHT OF EARLY DIAGNOSIS, EARLY INITIATION OF IMMUNOSUPPRESSIVE THERAPY AND MULTIDISCIPLINARY MANAGEMENT

[1]Ho Wai Siu*, [2]Robert O'Neill, [2]Matthew Tong, [1]JunHee Hong, [3]Carole A Harris, [4]Morteza Aghmesheh, [5]Hussein Soudy. *[1]St George Hospital, Sydney, Australia; [2]The Sutherland Hospital, Sydney, Australia; [3]1. St George Hospital, 2. University of New South Wales, Sydney, Australia; [4]1. The Wollongong Hospital 2. University of Wollongong, Wollongong, Australia; [5]1. St George Hospital 2. University of New South Wales, Sydney, Australia*

**Background** The use of immune checkpoint inhibitors (ICIs) against programmed cell death protein -1 (PD-1), its ligand (PD-L1) and cytotoxic T- lymphocyte associated protein 4 (CTLA4) have been increasing. Immune induced myocarditis, myositis and myasthenia gravis are rare but potentially severe complications from these agents. Here we report 3 cases of ICI induced myocarditis, myositis, myasthenia gravis and transaminitis as a cluster, and highlights early diagnosis, prompt initiation of steroid sparing immunosuppressive therapy and multidisciplinary management.

**Methods** Three patients received anti-PD-1 ICIs developed cardiac, neuromuscular complications and transaminitis within 4 weeks after initiation. Clinical data were retrospectively reviewed from medical records.

**Results** All patients had elevated cardiac enzymes, developed complete heart block and underwent coronary catheterisation and pacemaker insertion. All patients developed myositis and myasthenia gravis (table 1) and were managed by multi-disciplinary team involving oncology, cardiology and neurology. Single-fibre electromyography was performed to confirm presence of myositis. One of three patients had positive acetylcholinesterase antibody, anti- muscle specific kinase antibody was negative in all cases. All patients developed grade 2–3 transaminitis with normal bilirubin. All patients received high-dose steroids. Steroid sparing therapy including intravenous immunoglobulin and mycophenolate mofetil were used early in 2 cases and was associated with rapid recovery of toxicities.

**Abstract 292 Table 1** Patient characteristics, management and outcome of ir-AEs

| Age, gender and primary malignancy | ICI agent and time of onset | Signs and Symptoms | Treatment of toxicity | Outcome of ICI related toxicities |
|---|---|---|---|---|
| 81, M, advanced melanoma | Pembrolizumab, 4 weeks | Exertional dyspnoea Fatigue Diplopia | Prednisone 50mg daily IVIG | Ongoing deterioration |
| 74, M, resected melanoma | Nivolumab, 3 weeks | Dysphonia, dyspnoea, muscle weakness | Methylprednisolone 1g IVIG Mycophenolate mofetil | Recovered and discharged after 32 days |
| 63, M, advanced renal carcinoma | Pembrolizumab, 3 weeks | Chest pain, dyspnoea and lethargy | Methylprednisolone 1g IVIG Mycophenolate mofetil | Recovered and discharged after 20 days |

**Conclusions** ICI induced myocarditis can be associated with myositis, myasthenia gravis and transaminitis. A high index of suspicion, comprehensive investigations and early involvement of multi-disciplinary teams are key to early accurate diagnosis.