Table S1. **Treatment-Emergent Adverse Events (TEAE)** (data cut: 07-22-2020)

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| --- | --- | --- |
|  | **Vopratelimab MonotherapyN=70 (%)** | **Vopratelimab + nivolumab N=131 (%)** |
| **Preferred Term** | **Grade 1 & 2****n (%)** | **Grade ≥3****n (%)** | **Grade 1 & 2****n (%)** | **Grade ≥3****n (%)** |
| Subjects with at least one TEAE | 67 (95.7) | 39 (55.7) | 127 (96.9) | 63 (48.1) |
| fatigue | 20 (28.6) | 3 (4.3) | 47 (35.9) | 5 (3.8) |
| nausea | 17 (24.3) | 1 (1.4) | 45 (34.4) | 1 (0.8) |
| decreased appetite | 16 (22.9) | 3 (4.3) | 31 (23.7) | 3 (2.3) |
| pyrexia | 9 (12.9) | 0 | 29 (22.1) | 0 |
| dyspnoea | 9 (12.9) | 2 (2.9) | 25 (19.1) | 2 (1.5) |
| cough | 7 (10.0) | 0 | 26 (19.8) | 0 |
| infusion related reaction | 6 (8.6) | 1 (1.4) | 26 (19.8) | 0 |
| vomiting | 9 (12.9) | 1 (1.4) | 23 (17.6) | 0 |
| diarrhoea | 10 (14.3) | 4 (5.7) | 20 (15.3) | 2 (1.5) |
| constipation | 10 (14.3) | 0 | 20 (15.3) | 2 (1.5) |
| anaemia | 14 (20.0) | 8 (11.4) | 12 (9.2) | 7 (5.3) |
| hyponatraemia | 4 (5.7) | 6 (8.6) | 14 (10.7) | 13 (9.9) |
| back pain | 6 (8.6) | 0 | 18 (13.7) | 4 (3.1) |
| abdominal pain | 13 (18.6) | 2 (2.9) | 11 (8.4) | 2 (1.5) |
| dizziness | 12 (17.1) | 0 | 13 (9.9) | 0 |
| aspartate aminotransferase increased | 7 (10.0) | 4 (5.7) | 11 (8.4) | 6 (4.6) |
| arthralgia | 4 (5.7) | 0 | 18 (13.7) | 1 (0.8) |
| chills | 6 (8.6) | 0 | 16 (12.2) | 0 |
| headache | 5 (7.1) | 0 | 16 (12.2) | 1 (0.8) |
| weight decreased | 7 (10.0) | 1 (1.4) | 14 (10.7) | 0 |
| rash | 5 (7.1) | 0 | 12 (9.2) | 1 (0.8) |
| dehydration | 8 (11.4) | 1 (1.4) | 7 (5.3) | 2 (1.5) |
| dysphagia | 3 (4.3) | 0 | 11 (8.4) | 3 (2.3) |
| hypomagnesaemia | 6 (8.6) | 0 | 11 (8.4) | 0 |
| urinary tract infection | 3 (4.3) | 1 (1.4) | 13 (9.9) | 1 (0.8) |
| alanine aminotransferase increased | 7 (10.0) | 3 (4.3) | 7 (5.3) | 0 |
| myalgia | 3 (4.3) | 0 | 13 (9.9) | 0 |
| pleural effusion | 6 (8.6) | 1 (1.4) | 7 (5.3) | 2 (1.5) |
| oedema peripheral | 8 (11.4) | 0 | 7 (5.3) | 1 (0.8) |
| hypokalemia | 5 (7.1) | 2 (2.9) | 7 (5.3) | 1 (0.8) |
| pruritis | 7 (10.0) | 0 | 7 (5.3) | 0 |
| hypoalbuminaemia | 3 (4.3) | 2 (2.9) | 7 (5.3) | 2 (1.5) |
| blood bilirubin increased | 4 (5.7) | 1 (1.4) | 3 (2.3) | 6 (4.6) |

**Table S1 Legend:** TEAE includes any event not present prior to the initiation of the treatment(s) or already present that worsens in either intensity or frequency following exposure to treatment up to and including 28 days after last dose.

**Table S2 Legend:** 2Nivo: Nivolumab 240 mg q3w;3Geometric mean (geometric CV%) [n],Ctrough was only reported if a pre-dose sample was collected on C2D1.4Arithmetic mean (standard deviation) [n]; 5One subject assigned to 0.03 mg/kg vopratelimab actually received 0.3 mg/kg vopratelimab. PK parameters were summarized based on the dose actually received. NA: not applicable; NC: not calculated; ND: not determined (ie no data).

**Table S2. Pharmacokinetics**

|  |  |  |  |
| --- | --- | --- | --- |
| **Vopratelimab Dose (mg/kg)1** | **Other Treatment2** | **Vopratelimab Q3W (Cycle 1)** | **Nivolumab Q3W (Cycle 1)** |
| **Cmax3****(ng/mL)** | **Ctrough3****(ng/mL)** | **AUClast3****(ng·day/mL)** | **T1/24****(days)** | **Cmax3****(μg/mL)** | **AUC0-14d****(μg·day /mL)** |
| 0.003 | None | 59.8 (60.9%)[n=3] | 0.502(NC)[n=1] | 85.1(252%)[n=3] | 1.28(NC)[n=1] | NA |
| 0.01 | None | 179(15.4%)[n=3] | 3.32(NC)[n=1] | 493(16.9%)[n=3] | 1.16(0.0489)[n=2] | NA |
| Nivo | 251(25.7%)[n=3] | ND | 684(39.7%)[n=3] | 1.34(0.3100)[n=3] | 66.6(15.1%)[n=3] | 456(8.4%)[n=3] |
| 0.03 | None5 | 492(48.5%)[n=5] | 8.96(199.4%)[n=3] | 2260(206%)[n=5] | 3.25(1.313)[n=5] | NA |
| Nivo | 562(26.4%)[n=3] | 16.1 (3335%)[n=2] | 2460(95.6%)[n=3] | 2.46(NC)[n=1] | 63.4(11.9)[n=3] | 485(24.6%)[n=3] |
| 0.1 | None | 2070(31.4)[n=12] | 54.7(132%)[n=9] | 13,100(29.5%)[n=12] | 4.63(1.366)[n=12] | NA |
| Nivo | 2040(26.2%)[n=10] | 74.3(120%)[n=8] | 11,500(29.1%)[n=12] | 4.01(0.8497)[n=8] | 62.1(29.5%)[n=10] | 440(33.0%)[n=10] |
| 0.3 | None5 | 6250(25.6%)[n=11] | 468(265%)[n=9] | 45,000(41.2%)[n=11] | 5.18(2.095)[n=5] | NA |
| Nivo | 6210(20.9%)[n=15] | 461(183%)[n=12] | 36,500(31.0%)[n=15] | 5.46(2.442)[n=9] | 61.2(28.2)[n=15] | 390(30.3%)[n=15] |
| 1 | None | 18,400(22.5%)[n=6] | 3570(66.0%)[n=3] | 139,000(33.5%)[n=6] | 8.65(5.503)[n=2] | NA |

**Table S3 Legend:** Evaluable for response defined as subjects in safety analysis set who have a baseline tumor assessment, and either has at least one post-baseline tumor assessment scan and/or discontinued treatment due to death or disease progression. Similar trends observed with fresh pre-treatment tissue. 1n=22; 2n=67

**Table S3. ICOS and PD-L1 expression (IHC) using archival tissue does not track with clinical outcomes whereas TISvopra score does**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Overall Study Population (n=201)** | **ICOS** **IHC 2,3****n=106** | **ICOS** **IHC 0,1****n=57** | **PD-L1 TPS≥50%****n=11** | **PD-L1****TPS<50%****n=145** | **PD-L1 TPS≥1%****n=62** | **PD-L1 TPS<1%****n=94** | **TISvopra positive****n=22** | **TISvopra negative****n=67** |
| Evaluable for response, n (%) | 96 (90.6) | 50 (87.7) | 10 (90.9) | 130 (89.7) | 57 (91.9) | 83 (88.3) | 21 (95.5) | 62 (92.5) |
| ORR, n (%)95% CI | 2 (1.9)(0.2, 6.7) | 2 (3.5)(0.4, 12.1) | 0(0.0, 28.5) | 4 (2.8)(0.8, 6.9) | 1 (1.6)(0.0, 8.7) | 3 (3.2)(0.7, 9.0) | 3 (14.3)(3.1, 36.3) | 0(0.0, 5.8) |
| mPFS (mo)95% CI | 2 (1.9, 2.1) | 2(1.9, 2.0) | 1.5(0.3, 1.9) | 2(1.9, 2.0) | 1.9(1.8, 2.0) | 2.0(1.9, 2.1) | 2.21(2.0, 4.6) | 1.92(1.8, 2.0) |
| mOS (mo)95% CI | 9.4(6.8, 11.3) | 7.7(4.9, 9.3) | 6.2(3.2, 20.7) | 8.9(7.2, 9.9) | 7.8(6.6, 12.0) | 8.9(6.3, 10.3) | 16.91(9.1, 21.4) | 6.22(3.7, 9.0) |

1n=22; 2n=67

**Table S4 Legend: 1** Best Overall Response of Progressive Disease. NSCLC, non-small cell lung cancer; TNBC, triple negative breast cancer; HNSCC, head and neck squamous cell carcinoma

**Table S4. ICOS-hi/lo CD4 cell patient characteristics** (data cut: 07-22-2020)

|  |  |  |
| --- | --- | --- |
| **ICONIC Patient Characteristics** | **Vopratelimab Monotherapy** | **Vopratelimab + nivolumab** |
| **ICOS-hi n=4**  | **ICOS-lo n=6** | **ICOS-hi n=16** | **ICOS-lo n=18** |
| **Age (yrs), median (range)** | 55.5 (31.0, 75.0) | 67.0 (62.0, 70.0) | 63.0(43.0, 80.0) | 63.0 (37.0, 76.0) |
| **Prior therapies, median** | 3.0 | 2.5 | 3.0 | 3.0 |
| **≥3 prior therapies, n (%)** | 4 (100.0) | 3 (50.0) | 10 (62.5) | 10 (55.6) |
| **Prior immunotherapy, n (%)****prior PD-L1, n (%)****prior PD-1, n (%)** | 2 (50.0)02 (50) | 3 (50.0)03 (50.0) | 7 (43.8)1 (6.3)6 (37.5) | 7 (38.9)3 (16.7)4 (22.2) |
| **Refractory to prior immunotherapy1 n (%)** | 1 (50.0) | 1 (33.3) | 1 (14.3) | 4 (57.1) |
| **Tumor type, n (%)** | Gastric n=1 (25.0) | Gastric n=0 | Gastric n=8 (50.0) | Gastric n=7 (38.9) |
| NSCLC n=1 (25.0) | NSCLC n=0 | NSCLC n=4 (25.0) | NSCLC n=3 (16.7) |
| TNBC n=0 | TNBC n=0 | TNBC n=1 (6.3) | TNBC n=3 (16.7) |
| HNSCC n=0 | HNSCC n=0 | HNSCC n=1 (6.3) | HNSCC n=3 (16.7) |
| Other: neuroendocrine n=1 (25.0),prostate n=1 (25.0) | Other:cholangiocarcinoma n=1 (16.7), HNSCC n=2 (33.4), melanoma n=1 (16.7), sarcoma n=1 (16.7), TNBC n=1 (16.7) | Other:endometrial n=1 (6.3),cervical n=1 (6.3) | Other:ovarian n=1 (5.6),sarcoma n=1 (5.6) |