### SUPPLEMENTAL MATERIAL

### SUPPLEMENTAL TABLES AND FIGURES

**Supplemental table 1** Potential immune-mediated AEs (safety analysis set)

<table>
<thead>
<tr>
<th>n (%)</th>
<th>OCI 50 mg plus TIS 200 mg (n=1)</th>
<th>OCI 150 mg plus TIS 200 mg (n=3)</th>
<th>OCI 450 mg plus TIS 200 mg (n=6)</th>
<th>OCI 900 mg plus TIS 200 mg (n=16)</th>
<th>OCI 1800 mg plus TIS 200 mg (n=6)</th>
<th>Total (N=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colitis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Transaminases increased</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>0 (0.0)</td>
<td>1 (33.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Myositis</td>
<td>0 (0.0)</td>
<td>1 (33.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (6.3)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Rash</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (16.7)</td>
<td>1 (3.1)</td>
</tr>
</tbody>
</table>
maculopapular |   |   |   |   |   |

Data cutoff: September 29, 2022. The safety analysis set included all patients who received ≥1 dose of study drugs.

Abbreviations: AEs, adverse events; OCI, ociperlimab; TIS, tislelizumab.

### Supplemental table 2 Preliminary PK parameters of ociperlimab in Cycle 1 (PK analysis set*, n=32)

<table>
<thead>
<tr>
<th></th>
<th>t₁/₂ (days)</th>
<th>Tₘ₉ₓ (hr)</th>
<th>Cₘ₉ₓ (ug/mL)</th>
<th>C₉₅₉ (ug/mL)</th>
<th>AUCₘ₉ₓ (day·ug/mL)</th>
</tr>
</thead>
</table>
Serum samples of OCI were analyzed using a validated ELISA. Non-compartmental methods of PK analysis were used to derive PK parameters. The PK analysis set included all patients who received ≥1 dose of study drugs and had ≥1 derivable PK parameter.

*Only three of six patients in the 1800 mg cohort had reportable concentrations at the 28-day timepoint.

Abbreviations: \( \text{AUC}_{\text{inf}} \), area under the curve – infinity; \( C_{\text{max}} \), maximum concentration; \( C_{\text{trough}} \), trough concentration; \( \text{CV} \), coefficient of variation; ELISA, enzyme-linked immunosorbent assay; hr, hour; OCI, ociperlimab; PK, pharmacokinetic; \( t_{1/2} \), terminal half-life; TIS, tislelizumab; \( T_{\text{max}} \), time to reach \( C_{\text{max}} \).

**FIGURES**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Geometric mean (range)</th>
<th>Median (range)</th>
<th>Geometric mean (geometric CV%)</th>
<th>Geometric mean (geometric CV%)</th>
<th>Geometric mean (geometric CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCI 50 mg plus TIS 200 mg (n=1)</td>
<td>7.1 (7.1–7.1)</td>
<td>1.5 (1.5–1.5)</td>
<td>14.7 (1.5)</td>
<td>0.3 (1.5)</td>
<td>72.3 (1.5)</td>
</tr>
<tr>
<td>OCI 150 mg plus TIS 200 mg (n=3)</td>
<td>8.9 (7.8–11.0)</td>
<td>1.5 (1.5–24.0)</td>
<td>38.9 (33.5)</td>
<td>2.2 (1.5)</td>
<td>293 (19.1)</td>
</tr>
<tr>
<td>OCI 450 mg plus TIS 200 mg (n=6)</td>
<td>9.5 (6.3–14.8)</td>
<td>1.5 (1.5–1.5)</td>
<td>130.0 (19.1)</td>
<td>8.7 (109.0)</td>
<td>1090.0 (51.5)</td>
</tr>
<tr>
<td>OCI 900 mg plus TIS 200 mg (n=16)</td>
<td>10.9 (4.2–28.2)</td>
<td>1.5 (1.5–24.0)</td>
<td>263.0 (19.4)</td>
<td>21.0 (108.0)</td>
<td>2580.0 (39.0)</td>
</tr>
<tr>
<td>OCI 1800 mg plus TIS 200 mg (n=6)</td>
<td>9.0 (6.5–14.4)</td>
<td>1.5 (1.5–1.5)</td>
<td>526.0 (29.1)</td>
<td>31.2 (62.1)</td>
<td>4060.0 (34.4)</td>
</tr>
</tbody>
</table>
Supplemental figure 1 Study design

C, cycle; D, day; DLT, dose-limiting toxicity; IV, intravenous; Q3W, every 3 weeks.
The safety analysis set included all patients who received ≥1 dose of study drugs.

†The efficacy-evaluable analysis set included all patients who received ≥1 dose of study drugs, had evaluable disease at baseline, and ≥1 evaluable postbaseline tumor response assessment (unless any clinical progressive disease or death occurred before the first postbaseline tumor assessment).

‡The DLT-evaluable analysis set included patients who received at least 80% of the assigned doses of ociperlimab and tislelizumab (according to the treatment schedule), remained on study for the DLT observation period under sufficient safety evaluation, or who experienced a DLT within the observation period.

§The PK analysis set included all patients who received ≥1 dose of study drugs and had ≥1 derivable PK parameter.

DLT, dose-limiting toxicity; PK, pharmacokinetic.
**Supplemental figure 3** Mean serum concentration–time profiles of ociperlimab after first dose (PK analysis set*, n=32)

*Only three of six patients in the 1800 mg cohort had reportable concentrations at the 28-day timepoint. Serum samples of ociperlimab were analyzed using a validated ELISA. A non-compartmental method was used to derive PK parameters. The PK analysis set included all patients who received ≥1 dose of study drugs and had ≥1 derivable PK parameter. Data are presented as mean (±SD).

ELISA, enzyme-linked immunosorbent assay; PK, pharmacokinetic; SD, standard deviation.
**Supplemental figure 4** TIGIT receptor occupancy on peripheral CD8⁺ T cells at ociperlimab doses of 50–1800 mg

TIGIT receptor occupancy was determined from blood sample using FACS. The graph presents receptor occupancy data per patient as different colored lines.

C, cycle; CD, cluster of differentiation; D, day; FACS, fluorescence-activated cell sorting; hr, hour; PRE, pre-dose; RO, receptor occupancy; TIGIT, T-cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain.
## AdvanTIG-105 phase I dose escalation investigators list

<table>
<thead>
<tr>
<th>Name</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sophia Frentzas</td>
<td>Department of Medical Oncology, Monash Health, Melbourne, Victoria, Australia</td>
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<tr>
<td></td>
<td>Faculty of Medicine, Nursing and Health Sciences and School of Clinical Sciences, Monash University, Melbourne, Victoria, Australia</td>
</tr>
<tr>
<td>Steven Kao</td>
<td>Chris O'Brien Lifehouse, School of Medicine, University of Sydney, Sydney, New South Wales, Australia</td>
</tr>
<tr>
<td>Tarek Meniawy</td>
<td>Linear Clinical Research and the University of Western Australia, Nedlands, Western Australia, Australia</td>
</tr>
</tbody>
</table>
**Full inclusion and exclusion criteria**

**Inclusion criteria**

Each patient must meet all the following inclusion criteria to be considered eligible for participation in this study:

1. Signed informed consent form and able to comply with study requirements.
2. Age ≥18 years (or the legal age of consent) at the time the informed consent form is signed.
3. Histologically or cytologically confirmed unresectable locally advanced or metastatic solid tumors previously treated with standard systemic therapy or for which treatment is not available or not tolerated, and who have not received prior therapy targeting T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT).
   - Patients with hepatocellular carcinoma require Child-Pugh A classification before the first dose of study drugs.
4. ≥1 evaluable lesion per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1).
5. If available, archived, formalin-fixed paraffin-embedded (FFPE) tumor tissue sample (block or approximately 15 freshly cut unstained FFPE slides).
   - If archival tissue is unavailable, optional fresh baseline tumor biopsy is strongly recommended.
7. Adequate organ function as indicated by the following laboratory values during screening:
   a. Absolute neutrophil count ≥1.5 x 10⁹/L
   b. Platelet count ≥100 x 10⁹/L
   c. Hemoglobin ≥90 g/L, without blood transfusion or growth factor support ≥14 days before sample collection.
d. Serum creatinine ≤1.5 x upper limit of normal (ULN) or estimated glomerular filtration rate ≥60 mL/min/1.73 m² by Chronic Kidney Disease Epidemiology Collaboration equation
e. Serum total bilirubin ≤1.5 x ULN (≤3 x ULN for patients with Gilbert syndrome)
f. Aspartate aminotransferase and alanine aminotransferase ≤3 x ULN.

8. Females of childbearing potential must be willing to use a highly effective method of birth control for the duration of the study, and ≥120 days after the last dose of study drugs, and have a negative urine or serum pregnancy test ≤7 days of the first dose of study drugs.

9. Nonsterile males must be willing to use highly effective method of birth control for the duration of the study and for ≥120 days after the last dose of study drugs.

Exclusion criteria

Patients who meet any of the following criteria will be excluded from this study:

1. Active leptomeningeal disease or uncontrolled brain metastasis.
   - Patients with equivocal findings or with confirmed brain metastases are eligible if they are asymptomatic and radiologically stable without need for corticosteroids for ≥4 weeks before the first dose of study drugs.

2. Active autoimmune diseases or history of autoimmune diseases that may relapse, with the following exceptions:
   - Controlled type 1 diabetes
   - Hypothyroidism (provided it is managed with hormone-replacement therapy only)
   - Controlled celiac disease
   - Skin diseases not requiring systemic treatment (e.g., vitiligo, psoriasis, or alopecia)
• Any other disease that is not expected to recur in the absence of external triggering factors.

3. Any active malignancy ≤2 years before the first dose of study drugs, except for the specific cancer under investigation and any locally recurring cancer that has been treated with curative intent (e.g., resected basal or squamous cell skin cancer, superficial bladder cancer, or carcinoma in situ of the cervix or breast).

4. Any condition that required systemic treatment with either corticosteroids (>10 mg daily of prednisone or equivalent) or other immunosuppressive medication ≤14 days before the first dose of study drugs, with the following exceptions:
   • Adrenal replacement steroid (dose ≤10 mg daily of prednisone or equivalent)
   • Topical, ocular, intra-articular, intranasal, or inhalational corticosteroid with minimal systemic absorption
   • Short course (≤7 days) of corticosteroid prescribed prophylactically (e.g., for contrast dye allergy) or for the treatment of a non-autoimmune condition (e.g., delayed-type hypersensitivity reaction caused by contact allergen).

5. History of interstitial lung disease, noninfectious pneumonitis, or uncontrolled lung diseases, including but not limited to pulmonary fibrosis, acute lung diseases, etc.

6. Uncontrolled diabetes or >grade 1 laboratory test abnormalities in potassium, sodium, or corrected calcium despite standard medical management or ≥grade 3 hypoalbuminemia ≤14 days before the first dose of study drugs.

7. Severe chronic or active infections (including but not limited to tuberculosis infection) requiring systemic treatment ≤14 days before the first dose of study drugs.

8. Known history of human immunodeficiency virus infection.

9. Known history of or active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection except for the following:
• Patients with untreated chronic HBV or chronic HBV carriers whose HBV DNA is ≥500 IU/mL or patients with positive HCV RNA should be excluded. Inactive hepatitis B surface antigen carriers, treated and stable hepatitis B patients (HBV DNA <500 IU/mL), and cured hepatitis C patients (as defined by a positive HCV antibody test and negative HCV RNA test) may be enrolled.

10. Major surgical procedure, open biopsy, or significant traumatic injury ≤4 weeks before the first dose of study drugs or anticipation of need for major surgical procedure during the study.

11. Prior immunodeficiency, allogeneic stem cell transplantation, or organ transplantation.

12. Any of the following cardiovascular criteria:

- Cardiac chest pain, defined as moderate pain that limits instrumental activities of daily living, ≤28 days before the first dose of study drugs
- Symptomatic pulmonary embolism or other clinically significant episode of thromboembolic disease ≤28 days before the first dose of study drugs
- History of acute myocardial infarction ≤6 months before the first dose of study drugs
- History of heart failure meeting New York Heart Association Classification III or IV ≤6 months before the first dose of study drugs
- Ventricular arrhythmia ≥grade 2 in severity ≤6 months before the first dose of study drugs
- Cerebrovascular accident ≤6 months before the first dose of study drugs
- Uncontrolled hypertension: systolic pressure ≥160 mmHg or diastolic pressure ≥100 mmHg despite anti-hypertension medications ≤28 days before the first dose of study drugs.

13. History of severe hypersensitivity reactions to other monoclonal antibodies.
14. Chemotherapy, immunotherapy (e.g., interleukin, interferon, or thymosin), or investigational therapy ≤14 days or 5 half-lives (whichever is shorter) before the first dose of study drugs.
   - Received any herbal medicine or Chinese patent medicines used to control cancer ≤14 days before the first dose of study drugs.
15. Toxicities from prior therapy that have not recovered to baseline, ≤ grade 1, or stabilized, except for adverse events not considered a likely safety risk (e.g., alopecia, neuropathy, and specific laboratory abnormalities).
16. Live vaccine ≤4 weeks before the first dose of study drugs.
   - Seasonal vaccines for influenza are generally inactivated vaccines and are allowed. Intranasal vaccines are live vaccines and are not allowed.
17. Medical condition or alcohol or drug abuse or dependence that, in the investigator’s opinion, will be unfavorable for the administration of study drugs or will affect the explanation of drug toxicity or adverse events (AEs) or are likely to result in insufficient compliance with study procedures.
18. Concurrent participation in another therapeutic clinical study.
19. Any condition that requires treatment with prohibited or restricted concomitant medication or therapy, including, but not limited to concurrent anti-cancer therapy, live vaccine, immunosuppressive agents, systemic corticosteroids, alcohol abuse and other addictive drugs throughout the study, herbal remedies with immune-stimulating properties, radiation therapy, and non-steroidal anti-inflammatory drugs.

**Complete list of study endpoints for dose escalation part**

**Primary endpoints**

- AEs and serious AEs as characterized by type, frequency, severity (as graded by National Cancer Institute Common Terminology Criteria for Adverse Events [NCI-CTCAE] version 5.0), timing, seriousness, and relationship to study drugs; physical
examinations, electrocardiograms, and laboratory assessments as needed; and AEs meeting protocol-defined dose-limiting toxicity (DLT) criteria.

- Maximum tolerated dose (MTD) or maximum administered dose, as defined as the highest dose at which less than one-third of patients experienced a DLT or the highest dose administered, respectively.

- The recommended phase II dose of ociperlimab in combination with tislelizumab, determined by MTD or maximum administered dose, as well as long-term tolerability, pharmacokinetic, efficacy, and any other relevant data as available.

**Secondary endpoints**

- Overall response rate (ORR), duration of response (DoR), and disease control rate (DCR), as assessed using RECIST v1.1.

- Serum concentrations at specified timepoints and pharmacokinetics parameters of ociperlimab and tislelizumab.

- Immunogenic responses to ociperlimab and tislelizumab, evaluated through the detection of antidrug antibodies.

**Exploratory endpoints**

- Biomarkers from patient-derived tumor tissue(s) and/or blood (or blood derivative) samples obtained before, during, and/or after treatment with ociperlimab and their association with clinical efficacy. Biomarkers may include, but are not limited to, expression of TIGIT, CD226, CD155, CD112, and PD-L1 in tumor tissues, tumor mutation burden and gene mutations in tissue and blood, microsatellite instability status, immune cell subpopulations and gene expression profiling on peripheral blood and/or tumor tissues, and concentrations of cytokines and soluble proteins in plasma or serum.
Statistical analysis for the dose escalation part

- **Safety Analysis:** Safety will be determined by the spontaneous reporting of AEs and by laboratory values (hematology, clinical chemistry, coagulation, and urinalysis). Vital signs, physical examinations, and ECG findings will also be used in determining the safety profile. The severity of AEs will be graded according to NCI-CTCAE version 5.0. The incidence of treatment-emergent AEs (TEAEs) will be reported as the number (percentage) of patients with TEAEs by Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred term. Descriptive summary statistics (e.g., n, mean, standard deviation, median, minimum, and maximum for continuous variables; n [%] for categorical variables) and changes from baseline will be determined for laboratory parameters and vital signs.

- **Efficacy Analysis:** Efficacy will be based upon investigators' tumor assessments per RECIST version 1.1 and will be summarized with endpoints including ORR, DoR, and DCR to evaluate the preliminary anticancer activities of ociperlimab in combination with tislelizumab.