PEMBROLIZUMAB PLUS LENVATINIB VERSUS STANDARD OF CARE FOR PREVIOUSLY TREATED METASTATIC COLORECTAL CANCER: PHASE 3 LEAP-017 STUDY

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BACKGROUND

- The PD-1 inhibitor pembrolizumab is now recommended as a first- and subsequent-line treatment option for patients with microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) unresectable or metastatic colorectal cancer (mCRC)[1-4]
- For patients with non-MSI-H or MMR proficient (pMMR) mCRC, the current first-line standard of care (SOC) is a chemotherapy backbone that includes a fluoropyrimidine plus oxaliplatin and/or irinotecan, with or without vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR) inhibitors[1,2,5]
- There remains an unmet need for novel chemotherapy-free treatment options to improve survival outcomes of patients with non-MSI-H/pMMR CRC whose cancer progresses while on first-line therapy and those who cannot tolerate intensive chemotherapy[1,2,5]
- The combination of pembrolizumab with the multikinase inhibitor lenvatinib was shown to have promising antitumor activity and manageable safety in patients with previously treated non-MSI-H/pMMR CRC in the phase 2 LEAP-005 study[6]

OBJECTIVES

- To evaluate the efficacy and safety of pembrolizumab plus lenvatinib compared with investigator's choice of SOC therapy with regorafenib or TAS-102 in patients with non-MSI-H/pMMR mCRC that has progressed on or after prior treatment or who have become intolerant to prior treatment

Primary End Point

- Overall survival (OS)

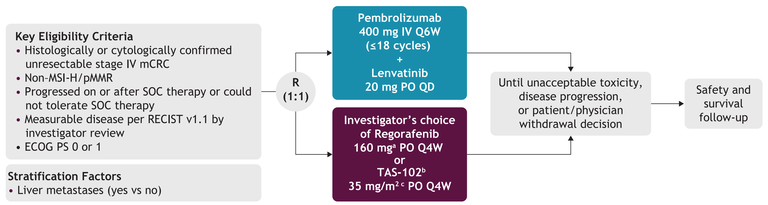
Secondary End Points

- Progression-free survival (PFS) per RECIST v1.1
- Objective response rate (ORR) per RECIST v1.1
- Duration of response (DOR) per RECIST v1.1
- Safety and tolerability
- Change from baseline in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) global health status and quality of life, physical functioning, and appetite loss scores, and EORTC Quality of Life Questionnaire-Colorectal Cancer-Specific 29 (QLQ-CR29) bloating scores
- Time to deterioration in EORTC QLQ-C30 global health status and quality of life, physical functioning, and appetite loss scores, and EORTC QLQ-CR29 bloating scores

METHODS

- LEAP-017 (NCT04776148) is a global, randomized, open-label, phase 3 trial

Figure 1. LEAP-017 Study Design



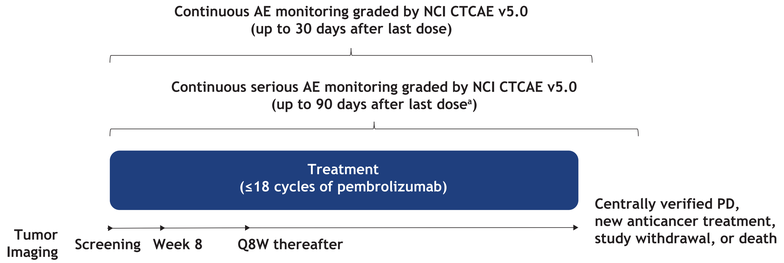
ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PO, orally; Q4W, every 4 weeks; Q6W, every 6 weeks; QD, daily.
[a]According to local guidelines, regorafenib may be administered as follows in cycle 1: 80 mg QD on cycle 1, days 1 to 7, then 120 mg QD on days 8 to 14, followed by 160 mg QD on days 15 to 21, and 160 mg QD on subsequent cycles (days 1 to 21; no doses days 22-28).
[b]TAS-102 is a combination of trifluridine and tipiracil hydrochloride.
[c]BID on days 1-5 and days 8-12; no doses on days 6 and 7 or days 13-28.

Table 1. Eligibility Criteria

Inclusion	Exclusion
• Patients aged ≥18 years • Histologically or cytologically confirmed unresectable and metastatic colorectal adenocarcinoma that is non-MSI-H/pMMR • Has been previously treated and has shown disease progression per RECIST v1.1[a] or could not tolerate standard treatment, which must include all the following agents if approved and available in the country of enrollment: – Fluoropyrimidine,[b] irinotecan, and oxaliplatin – With or without an anti-VEGF mAb – With anti-EGFR mAbs for *RAS* wild-type disease – BRAF inhibitor (plus cetuximab ± binimetinib) for *BRAF*^{V600E}-mutated mCRC • Measurable disease per RECIST v1.1 by investigator review • ECOG PS 0 or 1 • Has provided a newly obtained or archival tumor tissue sample • Adequate organ function • Blood pressure adequately controlled (≤150/90 mm Hg) with or without antihypertensive medications, with no change in antihypertensive medications for ≥1 week before randomization	• Gastrointestinal condition that may affect absorption • Radiographic evidence of encasement or invasion of a major blood vessel, or of intratumoral cavitation • Clinically significant hemoptysis or tumor bleeding ≤2 weeks before first dose of study drug • Clinically significant cardiovascular disease[c], ≤12 months before first dose of study drug • Preexisting grade ≥3 gastrointestinal or nongastrointestinal fistula • Active infection requiring systemic therapy • Active autoimmune disease that has required systemic treatment in the past 2 years, immunodeficiency, or under treatment with chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days before the first dose of study drug • History of HIV infection, hepatitis B (HBsAg reactive) infection, or active hepatitis C (HCV RNA detected) infection • History of noninfectious pneumonitis requiring steroids or current pneumonitis • Known CNS metastases and/or carcinomatous meningitis • Prior treatment with anti-PD-1/PD-L1/PD-L2 agents with anti-VEGF mAbs or VEGFR inhibitors, regorafenib, or TAS-102

CNS, central nervous system; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; mAbs, monoclonal antibodies; VEGFR, vascular endothelial growth factor receptor.
[a]Adjuvant chemotherapy counts as prior systemic therapy if there is documented disease progression ≤6 months after chemotherapy completion.
[b]Capecitabine is acceptable as an equivalent to fluoropyrimidine in prior treatment.
[c]Including New York Heart Association Class III or IV congestive heart failure, unstable angina, myocardial infarction, cerebral vascular accident, or cardiac arrhythmia associated with hemodynamic instability.

Figure 2. Assessments

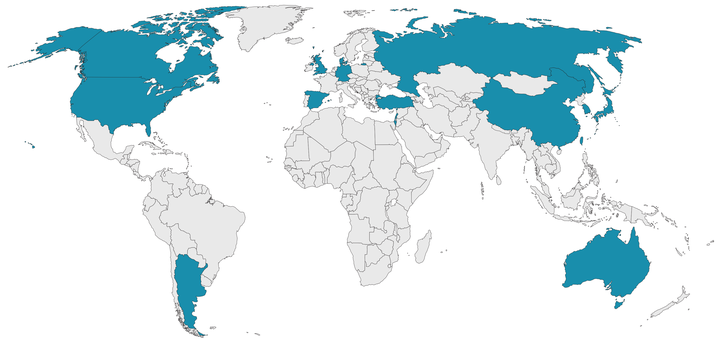


AE, adverse event; NCI CTCAE, v5.0, National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0; PD, progressive disease; Q8W, every 8 weeks.
[a]Assess for 30 days if a new anticancer treatment is initiated.

CURRENT STATUS

- Recruitment is ongoing at 117 sites in 15 countries/regions: Argentina, Australia, Canada, China, Denmark, Germany, Israel, Japan, Russia, South Korea, Spain, Taiwan, Turkey, the United Kingdom, and the United States
- Approximately 434 patients will be enrolled

Figure 3. Current Countries of Enrollment (in blue)



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Disclosures

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