First-Line Therapeutic Management of a Complex Gastric/GEJ Adenocarcinoma with Tislelizumab (Tevimbra®)

History and Initial Findings

A 58-year-old male patient, employed as a firefighter, presented in late 2024 with new-onset dysphagia that progressed markedly until Christmas 2024, ultimately resulting in severe swallowing impairment. His performance status was excellent (ECOG 0). He reported substantial unintentional weight loss of 16 kg over 3.5 months, with a current weight of 70 kg at a height of 180 cm.

The patient lives with his spouse and two children, smokes five cigarettes per day (previously ~10/day for 40 years), and consumes alcohol only rarely. Family history was unremarkable. No allergies were reported.

Past medical history included arterial hypertension treated with lisinopril/hydrochlorothiazide and a prior meniscal surgery.

Diagnostic Work-up and Tumor Characterization

Due to the rapidly worsening dysphagia, an oesophagogastroduodenoscopy was performed on December 30, 2024, revealing a subtotal stenosing, ulcerated tumor in the cardia region. Histology confirmed an adenocarcinoma of the cardia.

Subsequent staging with CT of the chest and abdomen demonstrated locoregional lymphadenopathy and multiple hypodense hepatic lesions.

A CT-guided liver biopsy on January 10, 2025, confirmed metastatic involvement consistent with the primary cardia carcinoma.

Comprehensive histopathological and molecular analysis yielded the following results:

- Moderately differentiated (G2) intestinal-type adenocarcinoma of the cardia
- Microsatellite stable (MSS)
- HER2-negative (1+)
- Claudin 18.2: 3+ in 90% of tumor cells
- PD-L1 CPS: 10
- PD-L1 TAP score: 10%

The diagnosis was therefore a subtotal-stenosing, G2 intestinal-type cardia adenocarcinoma with multiple liver metastases, corresponding to UICC stage IV in a palliative setting.

Treatment Decision and Clinical Course

The stenosis was successfully relieved by the gastroenterology team, allowing the patient to resume oral intake. The case was subsequently discussed at the interdisciplinary tumor board. Based on the overall clinical context, tumor biology, and evidence from the phase III RATIONALE-305 trial*, first-line palliative systemic therapy with capecitabine plus oxaliplatin (CapOx) in combination with the anti-PD-1 monoclonal antibody tislelizumab every three weeks was recommended. Subgroup analyses from RATIONALE-305 demonstrated benefit across all cohorts, including patients with hepatic and peritoneal metastases [1, 2].

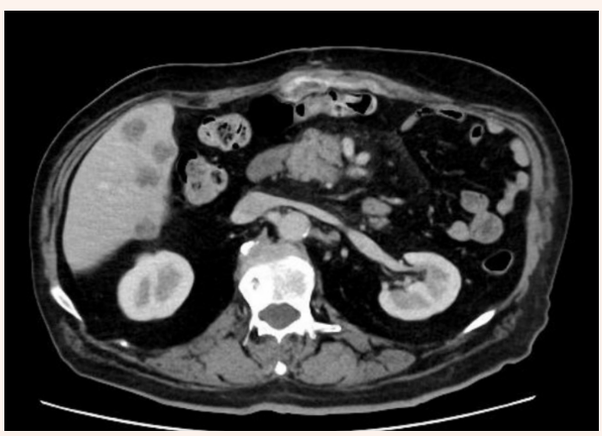

Fig. The presence of multiple hepatic metastases reflected the high therapeutic urgency prior to initiation of first-line palliative treatment with tislelizumab plus chemotherapy.

Treatment was initiated on February 3, 2025.

The regimen was generally well tolerated. The only notable toxicity was manageable grade I chemotherapy-induced peripheral neuropathy attributable to oxaliplatin; dose reduction was not required.

First restaging CT on May 7, 2025 showed a partial response. Clinically, the patient reported significant improvement and regained 3 kg of weight.

In line with the maintenance strategy used in RATIONALE-305, therapy was de-escalated after six cycles of CapOx + tislelizumab to tislelizumab plus capecitabine maintenance beginning mid-June 2025.

Tevimbra, in combination with platinum and fluoropyrimidine-based chemotherapy, is indicated for the first-line treatment of adult patients with HER-2-negative locally advanced unresectable or metastatic gastric or gastroesophageal junction (G/GEJ) adenocarcinoma whose tumours express PD-L1 with a tumour area positivity (TAP) score ≥ 5 %

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Follow-up CT imaging on August 6, 2025 under ongoing maintenance therapy demonstrated sustainable response.

Most notably, the most recent CT scan on November 10, 2025 revealed a radiological complete response.

The patient remains in ECOG 0 status, asymptomatic, fully active in daily life, and has regained weight to over 80 kg.

Assessment and Conclusion

This case describes an MSS cardia/gastric adenocarcinoma with high claudin 18.2 expression and moderate PD-L1 expression (CPS 10), presenting with hepatic metastases in a palliative context. The rapidly progressive symptoms and risk of complete obstruction created substantial therapeutic urgency requiring prompt initiation of systemic therapy.

Combination treatment with platinum-based chemotherapy (CapOx) and tislelizumab led to a rapid and pronounced tumor regression. Subsequent maintenance therapy with tislelizumab plus capecitabine resulted in durable disease control and, ultimately, radiological complete remission within nine months.

The patient currently enjoys excellent quality of life, has fully returned to work as a firefighter, and participates without limitation in social and daily activities.

References

1. Qiu, M., et al., Tislelizumab (TIS) + chemotherapy (chemo) vs placebo (PBO) + chemo as first-line (1L) treatment in gastric/gastroesophageal junction adenocarcinoma (GC/GEJC) patients with/without peritoneal or liver metastases: A post hoc analysis of RATIONALE-305 study. Journal of Clinical Oncology, 2025. 43(4_suppl): p. 414–414.
2. Qiu, M.Z., et al., Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first line treatment for advanced gastric or gastro-oesophageal junction adenocarcinoma: RATIONALE-305 randomised, double blind, phase 3 trial. BMJ, 2024. 385: p. e078876.

Summary of product characteristics, see page A16

*Randomized, placebo-controlled, double-blind Phase 3 study, NCT03777657, first-line therapy with tislelizumab + chemotherapy, locally advanced/unresectable/metastatic gastric or GEJ adenocarcinoma, N = 997