ESMO 2025 highlights
from BeOne Medicines

European Society For Medical Oncology

BeOne

Tislelizumab + chemotherapy (CT) in advanced GC/GEJC

Overall survival (OS) in patients who received 6 cycles of tislelizumab + CAPOX (capecitabine + oxaliplatin) and who continued capecitabine.[1]

Design highlights

997 treatment-naïve, HER2-negative advanced or metastatic gastric (GC) or gastro-oesophageal junction adenocarcinoma (GEJC)

R 1:1

6 cycles:
- Tislelizumab IV Q3W + CT* (n=501) → Continuation: + capecitabine (n=276); − capecitabine (n=45)
- Placebo IV Q3W + CT* (n=496) → Continuation: + capecitabine (n=250); − capecitabine (n=43)

*CT: oxaliplatin + capecitabine or cisplatin + 5-fluorouracil

Primary endpoint

OS in PD-L1-positive (PD-L1 TAP score ≥5%)

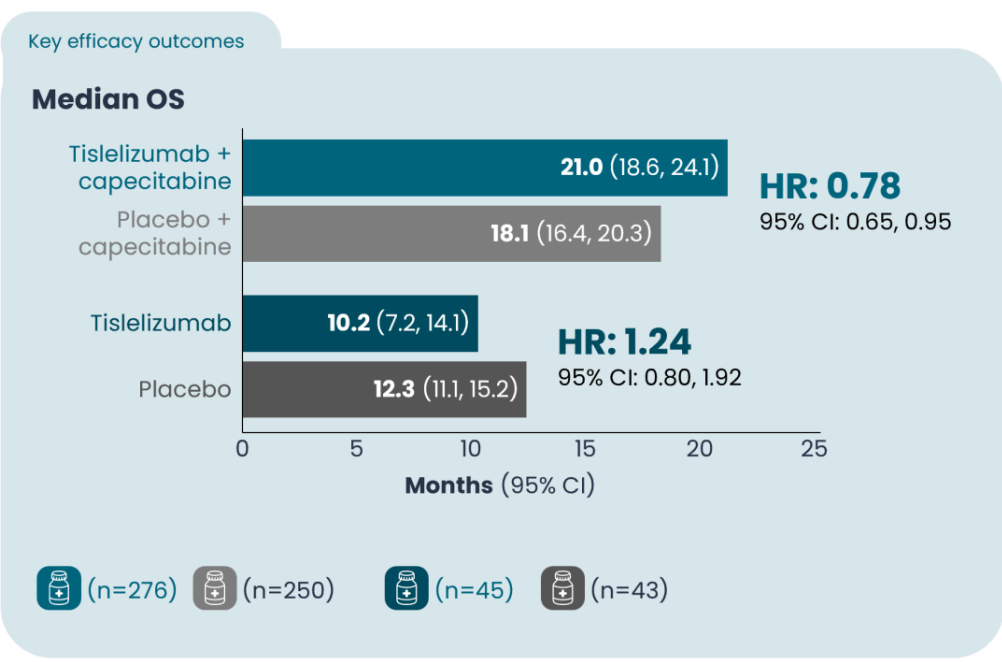
Secondary endpoints

PFS, DoR, ORR, Safety

Post hoc analysis

Tislelizumab + capecitabine continuation demonstrated significantly longer OS vs placebo + capecitabine continuation

Key efficacy outcomes



Key safety profile at the 3-year follow-up

Continuation of capecitabine with tislelizumab was generally well tolerated did not result in any new safety signals

	Tislelizumab + CT		Placebo + CT	Tislelizumab		Placebo
Patients with ≥1 TEAE	99.6%	vs	99.6%	100.0%	vs	100.0%
Patients with grade ≥3 TRAEs	55.1%	vs	53.2%	60.0%	vs	39.5%
TRAEs leading to discontinuation	16.3%	vs	7.6%	17.8%	vs	0.0%

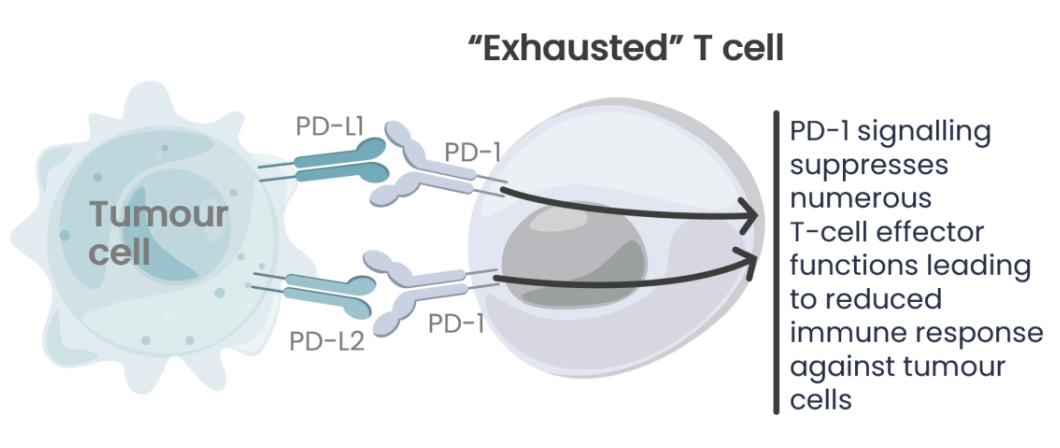
This post hoc analysis showed substantially longer OS in patients who continued capecitabine vs those who discontinued.[1]

Read the **RATIONALE-305** poster from Moehler *et al.*[1]

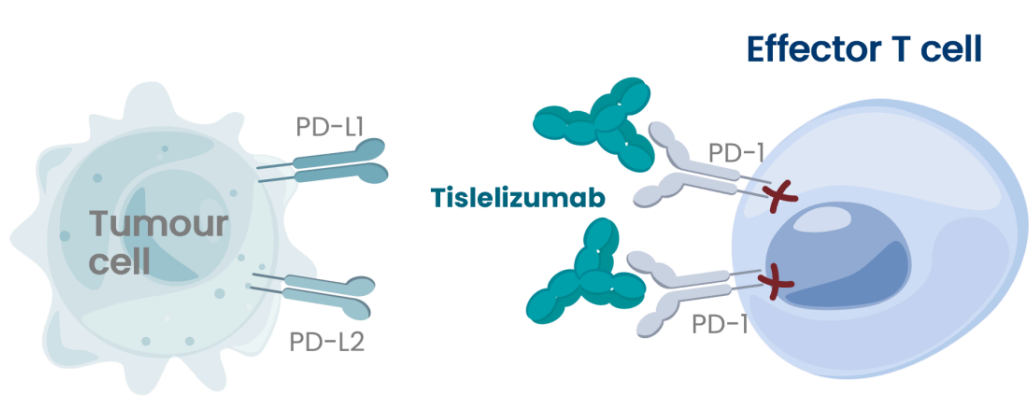
Spotlight on tislelizumab's mechanism of action

Prolonged exposure to cancer can result in T cell exhaustion, in which T cells have reduced effector functions and sustained expression of PD-1.[2,3]

Mechanism of action



Tislelizumab blocks the binding of both PD-L1 and PD-L2, helping to overcome T cell exhaustion.

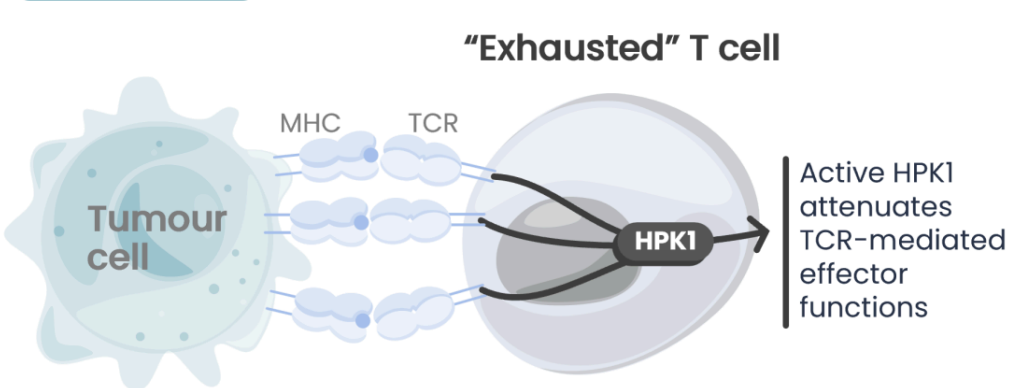


PD-1 and HPK1 inhibition can be combined

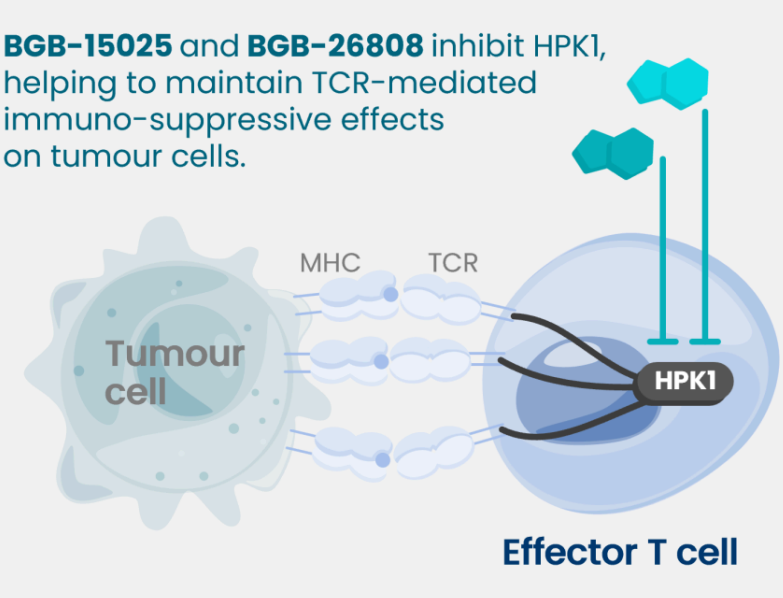
HPK1 is a negative feedback regulator in T cells that gets activated from continuous TCR engagement and that contributes to T cell exhaustion.[4-6]

Its mechanism of action is independent of the PD-1 pathway.[4]

Mechanism of action

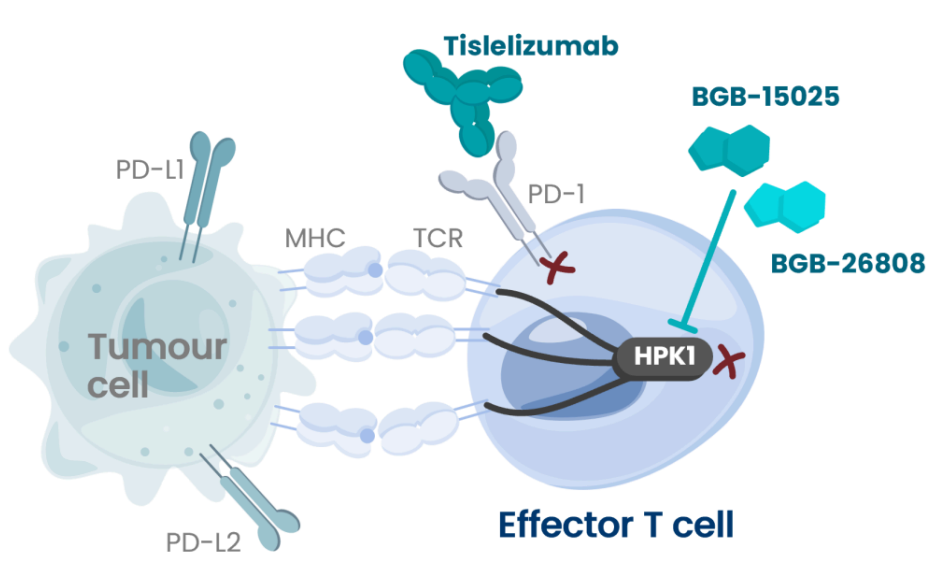


BGB-15025 and **BGB-26808** inhibit HPK1, helping to maintain TCR-mediated immuno-suppressive effects on tumour cells.



HPK1 signals independently of the PD-1.[x]

Targeting these 2 distinct pathways is currently being investigated in phase 1 trials to explore their potential synergetic effect



Combining HKN1 inhibitors with tislelizumab

BGB-15025, a new HKN1 inhibitor, showed preliminary safety and efficacy in a phase 1b study when combined with tislelizumab + CT.[5]

Design highlights

45 patients with locally advanced, unresectable or metastatic:

Treatment-naïve **NSCLC** (n=12)	Treatment-naïve **GC/GEJC** (n=20)	CPI-treated **ESCC** (n=13)
BGB-15025 + tislelizumab + CT Q3W	**BGB-15025** + tislelizumab + CT Q3W	**BGB-15025** + tislelizumab Q3W

10.9 months (range 0.7-24.8)
Median study follow-up in the overall population

Primary endpoint

ORR

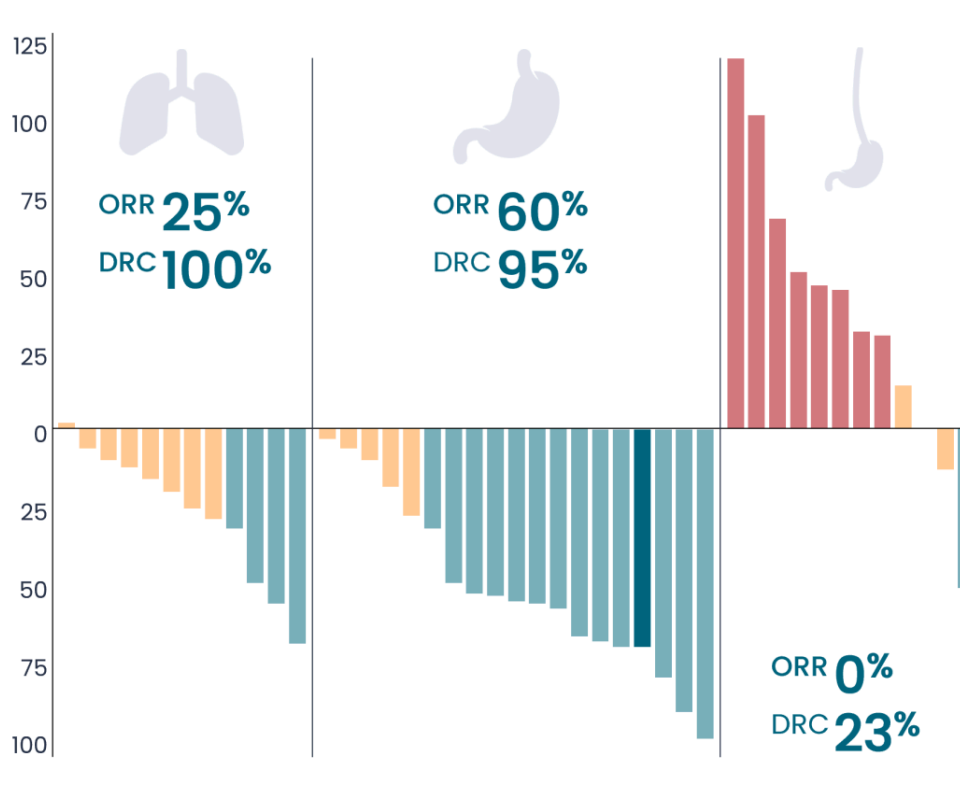
Secondary endpoints

PFS, DoR, DCR, Safety/tolerability

Key efficacy results

BGB-15025 + tislelizumab and chemotherapy demonstrated promising antitumor activity

Best overall response by investigator



Key safety and tolerability profile

The combination was generally well tolerated across these advanced solid tumour cohorts

	NSCLC	GC/GEJC	ESCC
Any treatment-related TEAE	100.0%	100.0%	61.5%
Grade ≥3 treatment-related TEAEs	66.7%	65.0%	15.4%
Treatment-related TEAEs leading to discontinuation	0.0%	15.0%	7.7%

TEAEs occurring in ≥30% of patients included: anaemia, neutrophil count decrease, AST increased, platelet count decreased, ALT increased and nausea.

The most common immune-mediated AE was skin rash.

Read the **phase 1 study** from Zhou *et al.*[5]

BGB-26808, a new HKN1 inhibitor, showed potential antitumor activity in advanced solid tumours in a phase 1a/b study when combined with tislelizumab.[6]

Design highlights

107 patients with advanced solid tumours who received between 1 to ≥6 prior lines of systemic therapies

	Part A Monotherapy	Part B Combination therapy
	BGB-26808 (n=55)	**BGB-26808 + Tislelizumab** QW3 (n=52)
Median follow-up	4.2 months (range 0.3-17.9)	4.3 months (range 0.5-16.3)

Key primary endpoint

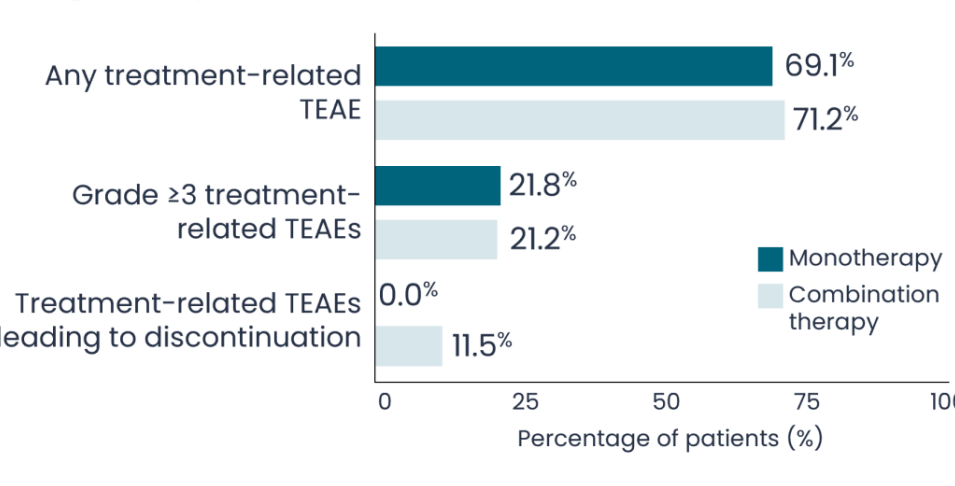
Safety and tolerability

Key secondary endpoints

ORR, DoR, DCR, CBR

Key safety and tolerability profile

BGB-26808 alone or in combination with tislelizumab was generally tolerable

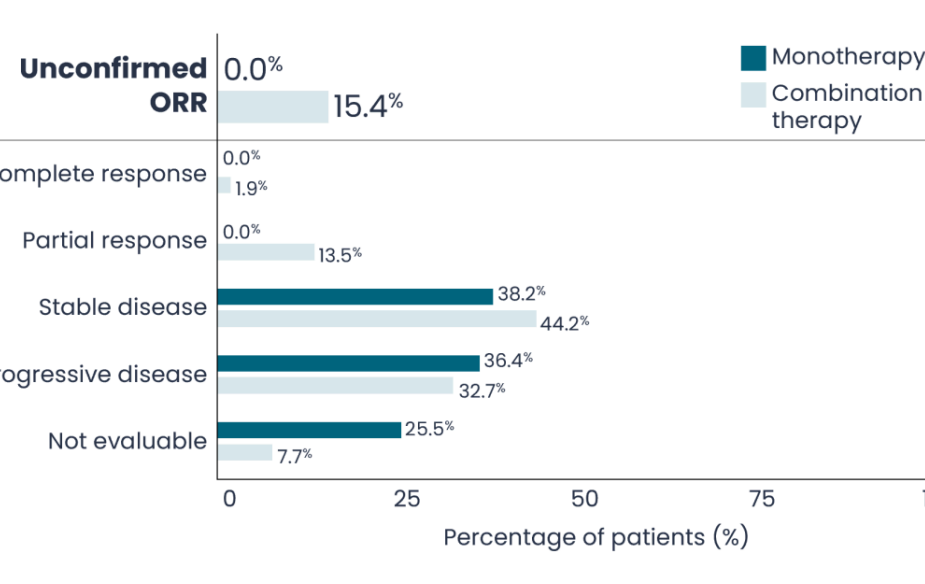


BGB-26808-related TEAEs in ≥10%: diarrhea, platelet count decreased, anaemia, AST increased, fatigue, nausea, vomiting, decreased appetite, lymphocyte count decreased and hypoalbuminemia.

The most common immune-mediated AE were rash and hypothyroidism.

Preliminary efficacy results

BGB-26808 in combination with tislelizumab showed potential antitumor activity



Read the **phase 1 study** poster from Naing *et al.*[6]

These 2 new HKN1 inhibitors showed potential antitumor activity when combined with tislelizumab and further investigation is ongoing.[5,6]

AE: adverse events; **AST**: aspartate aminotransferase; **CBR**: clinical benefit rate; **CT**: chemotherapy; **DCR**: disease control rate; **DoR**: duration of response; **ESCC**: oesophageal squamous cell carcinoma; **GC/GEJC**: gastric and gastro-oesophageal junction adenocarcinoma; **HR**: hazard ratio; **MHC**: major histocompatibility complex; **NSCLC**: non-small cell lung cancer; **ORR**: objective response rate; **OS**: overall survival; **Q3W**: once every 3 weeks; **PD-1**: programmed cell death protein 1; **PD-L1**: programmed death-ligand 1; **PD-L1 TAP**: PD-L1 tumour area positivity; **PFS**: progression-free survival; **TEAEs**: treatment-emergent adverse events; TRAEs: treatment-related adverse event; **TCR**: T cell receptor.

1. Moehler, M. et al. Tislelizumab With or Without Capecitabine Continuation in Gastric or Gastro-oesophageal Junction Cancer: RATIONALE-305 Post Hoc Analysis. Poster Presentation 2100P at ESMO; 17-21 October 2025; Berlin, Germany.
2. Tevimbra Summary Report on Authorisation. Swissmedic. 2024.
3. Nguyen, T.T., et al. (2025) Chronic Dis Transl Med 13;11(3):173-185.
4. Sawasdikosol, S. & Burakoff, S. (2020) eLife 9:e55122.
5. Zhou, C. et al. A First-in-Human, Phase 1 Study of BGB-15025 (Hematopoietic Progenitor Kinase 1 [HPK1] inhibitor) as Monotherapy and in Combination With Tislelizumab (anti-PD-1 Antibody) in Patients With Advanced Solid Tumors. Poster Presentation 1563P at ESMO; 17-21 October 2025; Berlin, Germany.
6. Naing, A. et al. First-in-Human, Phase 1 Study of BGB-26808 (Hematopoietic Progenitor Kinase 1 Inhibitor)± Tislelizumab in Advanced Solid Tumors. Poster Presentation 1564P at ESMO; 17-21 October 2025; Berlin, Germany.

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