RC118 combined with RC148 (ABBV-1480) for advanced gastric/gastroesophageal junction adenocarcinoma (G/GEJA): updated results from a randomized phase 2 trial

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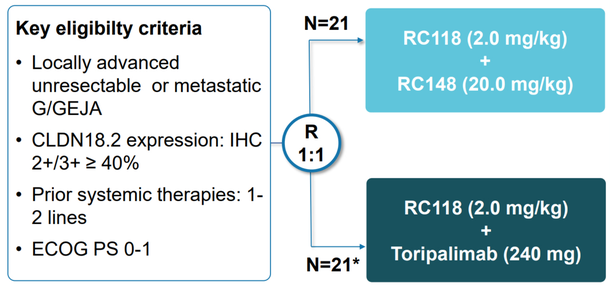
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BACKGROUND

- For patients with HER2-negative gastric or gastroesophageal junction adenocarcinoma (G/GEJA), second-line treatment of chemotherapy with or without anti-angiogenic agents offers an objective response rate (ORR) of 20%-28% and a median progression-free survival (PFS) of approximately 4 months, highlighting an unmet need for more effective treatment options.[1-3]
- RC118 (a CLDN18.2-targeted ADC) plus either RC148 (ABBV-1480, a PD-1/VEGF bispecific antibody) or toripalimab (Tor, a PD-1 inhibitor) showed promising ORR and manageable safety in CLDN18.2-positive pretreated advanced G/GEJA in the previous analysis of a phase 2 study.[4]
- We report here the updated efficacy and safety outcomes with a longer follow-up through July 26, 2026.

METHODS

Figure 1. Study design (NCT06038396)



- Randomization was stratified by PD-L1 CPS (≥1 vs <1).
- All study drugs were administered IV Q3W. Treatment was continued until disease progression, intolerable toxicity, consent withdrawal, or initiation of new anti-cancer treatment, whichever occurred first.
- Tumors were assessed as per RECIST v1.1 at baseline and thereafter every 6 weeks until disease progression, consent withdrawal, or initiation of new anti-cancer treatment, whichever came first.
- *One patient with pulmonary tuberculosis, who was initially misdiagnosed as postoperative recurrence with GC metastasis, was randomized to the RC118 + toripalimab group and was therefore excluded from the efficacy analysis but included in the safety analysis.

Endpoint

- Primary: ORR assessed as per RECIST v1.1, and safety.
- Secondary: DoR, DCR, PFS, OS, PK, and immunogenicity.

Abbreviations: PD-1: programmed death-1; VEGF: vascular endothelial growth factor; IHC: immunohistochemistry; ECOG PS: Eastern Cooperative Oncology Group performance status; R: randomized; IV: intravenously; Q3W: once every 3 weeks; PD-L1: programmed death-ligand 1; CPS: combined positive score; RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1; ORR: objective response rate; DoR: duration of response; DCR: disease control rate; PFS: progression-free survival; OS: overall survival; PK: pharmacokinetics; mo: months; NE: not estimable.

RESULTS

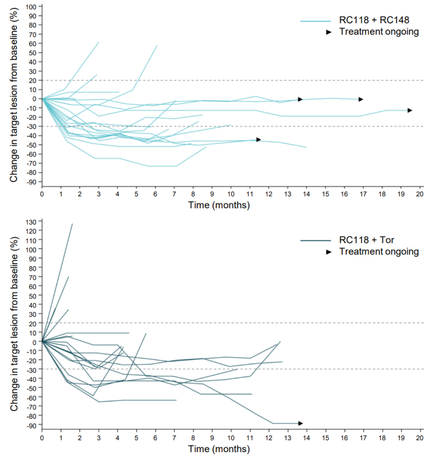
Patients

- Among the 42 randomized patients, 11 (52.4%) in the RC118 + RC148 group and 12 (57.1%) in the RC118 + Tor group had a CPS score <1; 16 (76.2%) and 15 (71.4%) had received prior PD-(L)1 therapy, respectively.
- The overall median follow-up duration was 14.6 months (95% CI: 13.0-16.9).

Antitumor activity

- Both RC118-containing combinations showed favorable and durable tumor response. The confirmed ORR (cORR) was 52.4% (95% CI: 29.8-74.3) with RC118 + RC148 and 35.0% (95% CI: 15.4-59.2) with RC118 + Tor. The median DoR was 7.0 (95% CI: 4.3-7.4) and 7.2 (95% CI: 3.0-NE) months, respectively.

Figure 2. Spider plot of tumor changes



- In the RC118 + RC148 group, DoR benefit was consistently observed across subgroups (Table 1).

Table 1. DoR with RC118 + RC148 – subgroup analysis

Subgroup	Median DoR (95% CI), mo
CPS <1	6.2 (4.3-NE)
CPS ≥1	7.2 (3.5-NE)
Prior PD-(L)1 treatment	7.0 (3.5-NE)
Presence of peritoneal metastasis	7.1 (5.3-NE)
Absence of peritoneal metastasis	6.5 (3.5-7.4)

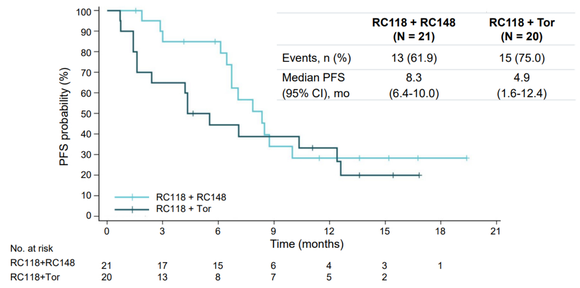
mo: months; NE: not estimable.

RESULTS

PFS

- The median PFS was 8.3 months (95% CI: 6.4-10.0) with RC118 + RC148 and 4.9 (95% CI: 1.6-12.4) with RC118 + Tor (Figure 3).

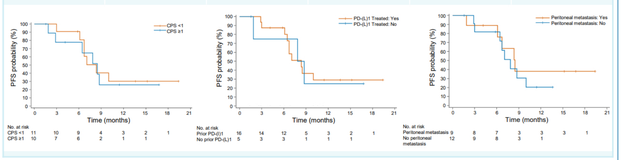
Figure 3. Progression-free survival



- In the RC118+ RC148 group, consistent PFS benefit was observed across subgroups (Table 2).

Table 2. PFS with RC118 + RC148 – subgroup analysis

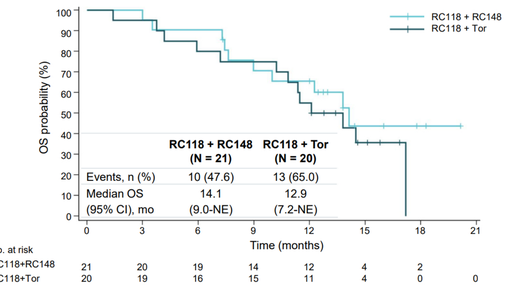
Median PFS (95% CI) with RC118 + RC148 Across Subgroups, mo					
CPS <1	CPS ≥1	Prior PD-(L)1 treatment	No prior PD-(L)1 treatment	Peritoneal metastasis	No peritoneal metastasis
8.3 (6.1-NE)	8.5 (1.9-NE)	8.3 (6.4-NE)	8.3 (1.9-NE)	8.5 (1.9-NE)	7.9 (3.0-10.0)



OS

- The median OS was 14.1 months (95% CI: 9.0-NE) with RC118 + RC148 and 12.9 (95% CI: 7.2-NE) with RC118 + Tor (Figure 4).

Figure 4. Overall survival



RESULTS

Safety

- The safety profiles for both groups were comparable and consistent with previous analysis (Table 3).[4]
- The most frequent (incidence ≥5.0% in either group) grade ≥3 treatment-related adverse events (TRAEs) were decreased appetite (9.5% vs 4.8%), lymphocyte count decreased (0 vs 9.5%), neutrophil count decreased (0 vs 9.5%), and white blood cell count decreased (0 vs 9.5%).
- The most frequent (incidence ≥5.0%) VEGF-related TRAEs in the RC118 + RC148 group were proteinuria (19.0%) and hypertension (19.0%), all being grade 1-2.

Table 3. Safety summary

n (%)	RC118 + RC148 (N=21)	RC118 + Tor (N=21)
Any TRAE*	21 (100)	20 (95.2)
≥ Grade 3	6 (28.6)	8 (38.1)
Serious	4 (19.0)	3 (14.3)
Leading to treatment discontinuation	2 (9.5)	2 (9.5)
Leading to death	0	0
Immune-related	3 (14.3)	2 (9.5)
≥ Grade 3	0	0
VEGF-related†	8 (38.1)	4 (19.0)‡
≥ Grade 3	0	0

*Related to any study drug. †Preferred terms related to VEGF. ‡All were proteinuria.

CONCLUSION

- With extended follow up, both RC118 combinations demonstrated manageable safety and favorable efficacy versus the standard treatment in patients with CLDN18.2-positive locally advanced or metastatic G/GEJA.
- RC118 + RC148 showed promising DoR and PFS benefits that were consistent across subgroups.
- A phase 2/3 study is in preparation to further evaluate the efficacy and safety of RC118 + RC148 in first-line G/GEJA.

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