PRIME-ROSE
Precision Cancer Medicine Repurposing System Using Pragmatic Clinical Trials

827P: Pertuzumab and Trastuzumab in HER2 overexpressed/ERBB2 amplified treatment refractory metastatic colorectal cancer. Merged data from patients treated in DRUP, FINPROVE, IMPRESS-Norway and ProTarget trials

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BACKGROUND

Colorectal cancer (CRC) is one of the most frequent cancers worldwide both in women and men (1). The median overall survival is up to 30 months, and the 5-year survival rate is approximately 20% for metastatic CRC in some of the subgroups (2).

CRC is a heterogenous disease with genetic and epigenetic aberrations in a complex tumor microenvironment (3). About 2-6% of CRC patients have a human epidermal growth factor receptor 2 (HER2) activated tumor, identified by HER2-overexpression by immuno-histochemistry or *ERBB2* amplification by genomic sequencing (4).

Although HER2-targeted therapies are FDA approved, and several studies have demonstrated clinical benefit in patients with HER2-positive/ *ERBB2*-amplified mCRC, these therapies have not yet been approved for this indication in Europe.

The objective of this study was to merge data from treatment refractory patients with HER2-positive/ *ERBB2*-amplified mCRC, who received therapy with trastuzumab and pertuzumab, in four precision oncology trials, DRUP, IMPRESS-Norway, FINPROVE and ProTarget. Our aim was to pool the data, to evaluate the response and survival of HER2-targeted therapy in a European patient population with HER2-positive/ ERBB2-amplified mCRC.

REFERENCES
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Figure 1

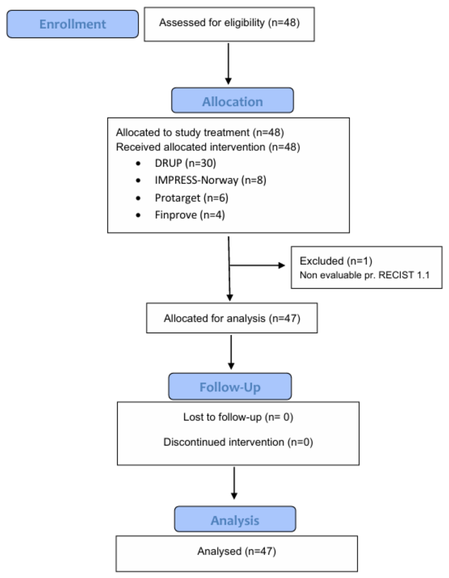

Figure 1A: Flow-chart of enrolled 48 enrolled patients. One patient was not evaluable according to RECIST, and final analyses were performed based on 47 patients.



Figure 1B: Waterfall plot of response at 16 weeks for 47 evaluable patients.

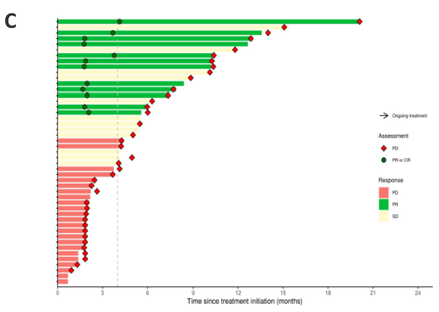

Figure 1C: Swimmers plot with initiation to end of therapy.

CONCLUSION

The study confirms a significant clinical benefit of trastuzumab and pertuzumab in patients with *ERBB2* amplified, standard treatment refractory mCRC.

The strength of this study is the successful merging of data from four trials. While the non-randomized, single-arm study design constitutes a limitation, the findings provide robust evidence supporting the efficacy of HER2-directed therapy for patients with HER2 overexpressed/ ERBB2-amplified mCRC.

METHODS

Data from four precision medicine trials within the Prime-Rose collaboration; DRUP (NCT02925234), FINPROVE (NCT05159245), IMPRESS (NCT04817956) and ProTarget (NCT04341181), were merged to assess the efficacy of HER2 directed therapy. Enrolled patients had treatment refractory mCRC with HER2 overexpression/*ERBB2* amplification and received trastuzumab plus pertuzumab. The primary endpoint was clinical benefit (CB), defined as an objective response or stable disease ≥ 16 weeks by RECIST 1.1 criteria.

RESULTS

A total of 48 patients were enrolled, with 47 evaluable for the primary endpoint. We found a CB rate of 51.1% (24/47) (95% CI, 0.38-0.64) and an objective response rate of 25.5% (12/47). The median duration of response was 7.5 months (95% CI, 5.4-NR). Median progression free survival (PFS) was 4.3 months (95% CI, 2.6-6.4) and median overall survival (OS) was 9 months (95% CI, 6.8-14.2). Two patients additionally had a *KRAS* mutation. The treatment was well tolerated, with only 8.3% (4/48) G3 treatment related adverse events.

Figure 2

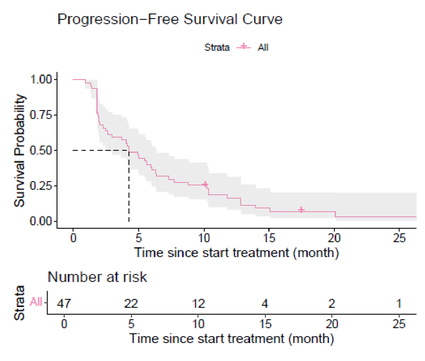

Figure 2A: Median progression free survival (PFS) was 4.3 months (95% CI, 2.6-6.4) .

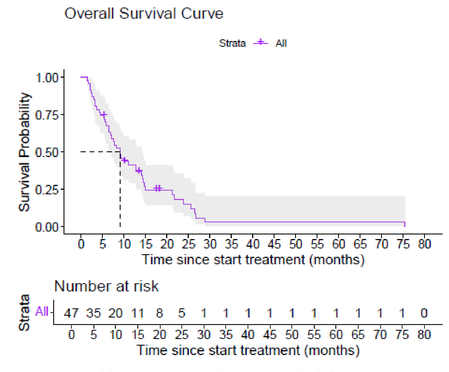

Figure 2B: Median overall survival (OS) was 9 months (95% CI, 6.8-14.2).

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