RWD110

Validation of Real-World Pathologic Complete Response in Early-Stage Triple Negative Breast Cancer

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Background

- Reliable real-world clinical outcome measures are needed to support health technology assessment (HTA), provider and regulatory decision-making in early-stage triple negative breast cancer (eTNBC).[1]
- Population-based studies have supported the potential of real-world pathologic complete response (rwpCR) as an effectiveness outcome. Nonetheless, there is a lack of evidence on validation of rwpCR compared to clinical trial pathological complete response (pCR) estimates.[2]

Objectives

This retrospective observational study examined the concordance between rwpCR and KEYNOTE-522 trial control (chemotherapy only) arm pCR estimates.

Methods

- Electronic health records from the US Oncology Network were used to identify patients with stage II-III TNBC who initiated neoadjuvant chemotherapy between 1/1/20 and 3/31/22. Patients were followed through 07/18/23.
- Patients treated with immunotherapy at any time were excluded.
- Real-world proxies for trial eligibility criteria were developed and applied to identify a real-world cohort matching KEYNOTE-522.
- Differences in available baseline demographic and clinical characteristics between the KEYNOTE-522 control arm population and the real-world cohort were adjusted through the Matching-Adjusted Indirect Comparison (MAIC) method.
- rwpCR and KEYNOTE-522 control arm pCR were compared using generalized linear models before (crude) and after MAIC was applied (adjusted).

Figure 1: Patient population attrition

Patients newly diagnosed with Stage II-III TNBC prior to 31 March 2022 (n=1379) in pre-curated data

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Started neoadjuvant treatment and did not receive neoadjuvant or adjuvant IO from 01 January 2020 to 31 March 2022 (n=501)

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Random subsample (n=400) underwent custom chart abstraction to apply clinical trial eligibility (i.e. confirmed TNM stage, ECOG, exclude autoimmune disease, exclude active infections) resulting in the study real-world cohort (n=199)

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Results

- Real-world patients (n=199) were older than KEYNOTE-522 trial participants (median age 59 vs 48 years), had more advanced disease (61% vs 25% stage III), and were more often ECOG>0 (40% vs 13).
- In unadjusted analyses, real-world patients were 15% less likely to achieve pCR when compared to patients in the control arm, though this difference was not statistically significant (RR: 0.85, 95% CI: 0.69, 1.05, p=0.125)
- After adjustment for age, race, ethnicity, clinical stage at diagnosis, and ECOG, there was greater concordance between the real-world cohort rwpCR and the KEYNOTE-522 control arm pCR (RR: 0.92, 95% CI: 0.75 – 1.13, p=0.422).

Table 1: Demographic and Clinical characteristics for trial and real-world patients with eTNBC

Variable	KEYNOTE-522 control group	Real-world cohort (crude)	Real-world cohort (adjusted)
Number of Patients	390	199	199
Age group at index (years), N (%)			
< 65	342 (88%)	142 (71%)	180 (90%)
>= 65	48 (12%)	57 (29%)	19 (10%)
Race, N (%)			
White/Caucasian	242 (62%)	118 (59%)	140 (71%)
Other	117 (30%)	59 (30%)	44 (22%)
Not documented	31 (8%)	22 (11%)	14 (7%)
Ethnicity, N (%)			
Hispanic, Latino/a, Spanish origin	39 (10%)	13 (7%)	18 (9%)
Not Hispanic, Latino/a, Spanish origin	307 (79%)	155 (78%)	158 (79%)
Not documented	44 (11%)	31 (16%)	23 (12%)
Clinical Cancer Stage at Initial Diagnosis, N (%)			
Stage I, Stage II	292 (75%)	116 (58%)	148 (74%)
Stage III	98 (25%)	83 (42%)	51 (26%)
ECOG, N (%)			
0	341 (87%)	120 (60%)	176 (88%)
1	49 (13%)	79 (40%)	23 (12%)

Table 2: Summary of rwpCR compared to pCR from KEYNOTE-522 clinical trial control arm

Cohort	Events (numerator) No. of Patients with pCR	Total (denominator) No. of Patients in the group	Risk Ratio			P-value
			Point estimate	95% Lower limit	95% upper limit	
Published Clinical trial control arm	103	201				
Real-world cohort (crude)	83	191	0.85	0.69	1.05	0.125
Real-world cohort (adjusted)	83	191	0.92	0.75	1.13	0.422

Note: 8 patients in the real-world cohort were excluded from these analyses because they underwent surgery but had no record of pCR (Yes or No)

Conclusions

By applying real-world definitions to match key study design elements with the KEYNOTE-522 trial and leveraging curated real-world data from The US Oncology Network, this study demonstrated that real-world pathologic complete response is concordant with clinical trial control arm estimates in eTNBC. These results increase confidence in the validity of real-world outcomes for early-stage breast cancer.

Limitations

- Though confounding was addressed through careful design and MAIC analyses, this study may be limited by unmeasured confounding between real-world cohorts and KEYNOTE-522 trial groups.
- Though excluding post-index immunotherapy patients was done to align the real-world population with the control arm of the trial and reduce misclassification, it likely introduced selection bias, which will be addressed in the next study phase though trial emulation methodology.
- Real-world data are subject to misclassification of treatments, patient factors and outcomes.
- The US Oncology Network and non-network practices serve diverse patients, nonetheless, results from this study are most generalizable to other community oncology practices that adhere to evidence-based treatment guidelines.

Contact information
Contact Dr. Desai at kaushal.desai@merck.com for questions and comments

Disclosures
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References

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