Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive or HER2-low-expressing advanced breast cancer and central nervous system involvement: Preliminary results from the DEBRA2 phase 2 study

BACKGROUND

- Approximately 30% to 35% of patients with human epidermal growth factor receptor 2-positive (HER2-positive) advanced breast cancer (ABC) have central nervous system (CNS) involvement.
- Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate containing monomethyl auristatin E payload and the fully humanized HER2 antibody, with similar amino acid sequence to trastuzumab and a potentially reduced risk of infusion-related reactions.

METHODS

- Recruitment and patient disposition
  - Median age: 50 years (range, 20–82)
  - Median ECOG performance status (PS): 0
  - 74.2% were male
  - Baseline characteristics were similar across cohorts

- Study design
  - Open-label, phase 2, multi-site, multi-arm study
  - Pts with HER2-positive or HER2-low-expressing advanced ABC with CNS involvement were enrolled in 5 cohorts

- Primary endpoints
  - Disease control rate (DCR; complete response [CR] + partial response [PR] + stable disease [SD])
  - CNS-PFS (assessed by RANO-BM criteria)

- Exploratory endpoints
  - CNS-PFS (assessed by RANO-BM criteria)
  - CNS-PFS per investigator

OBJECTIVE

- To assess the efficacy and safety of T-DXd in HER2(+) or HER2(-) ABC pts with CNS involvement and/or leptomeningeal carcinomatosis (LMC) with or without intracranial involvement

STUDY DESIGN

Figure 1. Study Design of DEBRA2 (NCT04202096)

RESULTS

1. Recruitment and patient disposition

Cohort 1: N=10 (median age 57 years, 70% female)
- 8 pts had HER2(+) ABC
- 2 pts had HER2(-) ABC

Cohort 2: N=9 (median age 54 years, 89% female)
- 8 pts had HER2(+) ABC
- 1 pt had HER2(-) ABC

Cohort 3: N=10 (median age 53 years, 100% female)
- 9 pts had HER2(+) ABC
- 1 pt had HER2(-) ABC

Cohort 4: N=10 (median age 50 years, 90% female)
- 9 pts had HER2(+) ABC
- 1 pt had HER2(-) ABC

Cohort 5: N=9 (median age 52 years, 94% female)
- 8 pts had HER2(+) ABC
- 1 pt had HER2(-) ABC

2. Efficacy in cohort 3

- 14 (41.2%) patients had measurable CNS disease
- 11 patients experienced SD
- 8 patients experienced PD

3. CNS-PFS (n=9)

- Median CNS-PFS: 8 months (95% CI, 2.1–11.2)
- 5 patients had progression in CNS
- 3 patients had progression outside CNS

4. CNS-PFS (n=10)

- Median CNS-PFS: 7 months (95% CI, 3.7–10.8)
- 5 patients had progression in CNS
- 5 patients had progression outside CNS

5. CNS-PFS (n=10)

- Median CNS-PFS: 7 months (95% CI, 3.7–10.8)
- 5 patients had progression in CNS
- 5 patients had progression outside CNS

6. CNS-PFS (n=10)

- Median CNS-PFS: 7 months (95% CI, 3.7–10.8)
- 5 patients had progression in CNS
- 5 patients had progression outside CNS

7. CNS-PFS (n=10)

- Median CNS-PFS: 7 months (95% CI, 3.7–10.8)
- 5 patients had progression in CNS
- 5 patients had progression outside CNS

8. CNS-PFS (n=10)

- Median CNS-PFS: 7 months (95% CI, 3.7–10.8)
- 5 patients had progression in CNS
- 5 patients had progression outside CNS

REFERENCES


CONCLUSIONS

- T-DXd demonstrated promising efficacy with manageable toxicity in pretreated ABC pts with HER2(+)/HER2(-) ABC with leptomeningeal involvement or intracranial involvement.
- Further investigation is required in larger cohorts to validate these findings and provide more complete evidence on the activity and safety of T-DXd for intracranial and extracranial disease in HER2(+) BC and HER2(-) BC.

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