Real-world HER2-positive unresectable or metastatic breast cancer treatment patterns and outcomes in China

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Objective

- To describe the treatment patterns in patients with HER2-positive unresectable or metastaic Breast Cancer (mBC) in China.
- To describe the demographic and baseline clinico-pathological characteristics of patients with HER2-positive unresectable or mBC.
- To describe the effectiveness of different treatment regimens for HER2-positive unresectable or mBC.

Conclusions

- This study outlines the clinical landscape and efficacy of treatments for HER2+ mBC in China.
- In 1L, dual anti-HER2 blockade mABs were preferred, while TKIs were the dominant choice.
- Real-world efficacy data from both 1L and 2L treatment underscore the significant unmet needs in these therapeutic lines.

Plain Language Summary

Why did we perform this research?
Anti-HER2 therapy for metastatic breast cancer (mBC) has rapidly evolved in China, with several new drugs approved in recent years. The treatment landscape in China differs from global standards, with high adoption of pyrotinib, recommended in both 1L treatment (pyrotinib+ trastuzumab+ chemotherapy) and 2L treatment (pyrotinib + chemotherapy). This study provides an overview of the current treatment landscape and efficacy following the introduction of these new anti-HER2 therapies.

How did we perform this research?
We retrospectively analyzed medical data from patients newly diagnosed with HER2+ metastatic breast cancer between January 2020 and August 2022.

What were the findings of this research?
The treatment choice for anti-HER2 regimens in China differed, emphasizing the high adoption of TKI, and showed the real-world efficacy of anti-HER2 therapy in mBC.

What are the implications of this research?
Our findings identified the real-world usage of treatments in China. The efficacy results highlight the unmet need in metastatic breast cancer, indicating that more effective therapies are needed earlier in patient care.

Where can I access more information?
ClinicalTrials gov (NCT05769751)

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Introduction

- Approximately 25% of breast cancer patients have an amplification of the human epidermal growth factor receptor-2 (HER2) expression in China[1-2], which is associated with aggressive tumor behavior.
- Currently, the global standard of care for HER2-positive (HER2+) mBC includes pertuzumab plus trastuzumab and chemotherapy for first-line (1L) treatment and trastuzumab deruxtecan for second-line (2L)[3-4].
- However, the treatment landscape in China differs:
  - Pyrotinib, an oral TKI, plays a crucial role in managing HER2+ mBC in China with phase III PHOEBE and PHILA trial[5-6].
  - The rapid approval of multiple anti-HER2 agents in mBC contributes to the evolving landscape of anti-HER2 therapy in Chinese breast cancer treatment.
  - The diverse array of treatment options in China has resulted in a growing divergence in clinical practices for breast cancer management compared to global standards.
- The real-world data on their use and efficacy in China is limited, especially following the approval of new drugs.

Methods

Study Design:

- This study was a multicenter, non-interventional, retrospective study (NCT05769751) conducted in five cancer centers across China.
- The study included 865 patients aged over 18 who were newly diagnosed with HER2-positive breast cancer that was unresectable or metastatic between January 1, 2020 and August 31, 2022, and who had received at least one round of systemic treatment. Patients with other malignancies, or participation in unblinded clinical trials were excluded.
- The primary outcome was real-world treatment patterns, defined as the distribution and sequence of various systemic therapy regimens across different treatment lines. The secondary outcome was, the real-world progression-free survival (rwPFS), assessed the time from the onset commencement of the current treatment line to documented disease progression or death, whichever occurred first.

Statistical Analysis:

- There was no hypothesis planned as it's a real world study.
- Descriptive analyses were performed on demographic and clinical characteristics, treatment patterns, and treatment outcomes in patients.
- Sankey diagrams were created to visualize the sequence of systemic therapy regimens between treatment lines.
- rwPFS along was estimated using the Kaplan-Meier methods. Results were reported as median rwPFS with 95% confidence intervals (CIs).

Results

- A total of 865 patients with newly diagnosed unresectable or metastatic Breast Cancer (mBC) were included in the study.

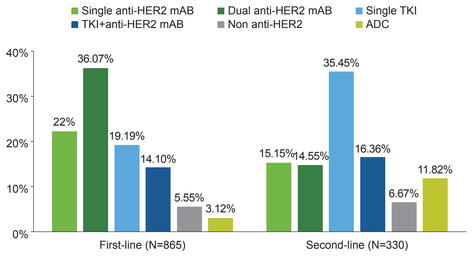
Table 1 Patient Characteristic

Characteristics	Value (N = 865)
Age (year)	
Mean (SD)	52.37 (10.52)
Median [Q1, Q3]	53.00 [45.67, 58.54]
Min, Max	21.87, 86.30
Age group (year), No. (%)	
<35	63 (7.28)
[35,65)	698 (80.69)
≥65	104 (12.02)
Sex, No. (%)	
Female	865 (100.00)
Family history of breast cancer, No. (%)	
Yes	76 (8.79)
No	657 (75.95)
Unknown	132 (15.26)
Menopausal status, No. (%)	
Post-menopausal	482 (55.72)
Pre-menopausal	314 (36.30)
Unknown	69 (7.98)
Eastern Cooperative Oncology Group performance status, No. (%)	
0-1	495 (57.23)
2-3	17 (1.97)
Missing	353 (40.81)
Disease history at initial diagnosis, No. (%)	
De novo mBC	321 (37.11)
Recurrent mBC	544 (62.89)
Time from the end of (neo)adjuvant treatment to recurrence by group, No. (%)	
<6 months	120 (26.79)
≥6 months	328 (73.21)
Site of primary lesion, No. (%)	
Left breast	447 (51.68)
Right breast	402 (46.47)
Bilateral breasts	16 (1.85)
Distant metastasis, No. (%)	
Yes	850 (98.20)
No	15 (1.80)
Visceral Disease, No. (%)	
Yes	548 (63.65)
No	313 (36.35)
Number of metastatic sites, No. (%)	
1	394 (45.55)
2	251 (29.02)
≥3	220 (25.43)
Selected metastatic sites, No. (%)	
Bone	366 (42.31)
Lung	344 (39.77)
Liver	304 (35.14)
Brain	95 (10.98)
HR status[a], No. (%)	
Positive	458 (53.26)
Negative	388 (45.12)
Undetected	14 (1.63)
HER2 status[a], No. (%)	
0	6 (0.70)
1+	6 (0.70)
2+	208 (24.19)
3+	622 (72.33)
Missing	18 (2.09)
Follow-up (month)	
Mean (SD)	13.56 (8.54)
Median [Q1, Q3]	12.84 [6.08, 19.96]
Min, Max	0.05, 32.02

[a] The most closely pathological result from the baseline.

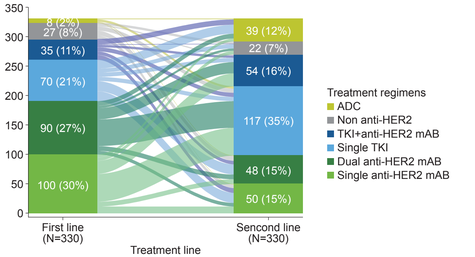
- 865 (100.00%) received at least 1 line of systemic therapy for mBC. In our data set, 38.15% had 2L treatment information, and 15.03% had post-2L treatments.
- Considering the complexity of real-world usage, the anti-HER2 treatments were categorized into six groups:
  - Dual anti-HER2 blockade monoclonal antibodies (Dual mAB): 98.45% of cases were treated with trastuzumab + pertuzumab.
  - Single anti-HER2 blockade mAB-based therapy (Single mAB): 83.39% were treated with trastuzumab, and 15.88% with inetetamab.
  - Single Tyrosine Kinase Inhibitor (TKI)-based therapy (Single TKI): 95.33% were treated with pyrotinib, and 3.73% with lapatinib.
  - TKI + anti-HER2 blockade mAB-based therapy (TKI + mAB): 77.45% received pyrotinib + trastuzumab, and 22.55% received pyrotinib + inetetamab.
  - Antibody-drug conjugates (ADCs): The top 3 ADC therapies were T-DM1 (29.82%), disitamab vedotin (14.91%), and ARX788 (11.4%).
  - Non-anti-HER2 therapy.
- The prominent medications were trastuzumab (83.39% of single mAB), trastuzumab plus pertuzumab (98.45% of dual mAB), and pyrotinib (95.33% of single TKI).
- The detailed treatment choices in the first line and second line were shown in **Figure 1**

Figure 1 Treatment patterns across first-line and second-line



- The transition patterns of anti-HER2 therapy from 1L to 2L were shown in **Figure 2**
- The predominant treatment option following single or dual anti-HER2 mAB was TKI. Post-TKI therapy typically involved either anti-HER2 mABs (dual or single) or ADCs.

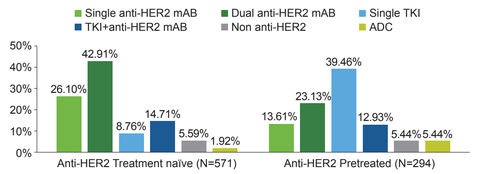
Figure 2 Treatment sequence from first-line to second-line treatment among patients who received at least two lines of systemic treatment



First-line No. (%)	Second-line No. (%): Single anti-HER2 mAB	Dual anti-HER2 mAB	TKI+anti-HER2 mAB	Single TKI	Non anti-HER2	ADC	Total No. (%)
Single anti-HER2 mAB	12 (3.64)	8 (2.42)	22 (6.67)	47 (14.24)	6 (1.82)	5 (1.52)	100 (30.30)
Dual anti-HER2 mAB	6 (1.82)	8 (2.42)	19 (5.76)	45 (13.64)	4 (1.21)	8 (2.42)	90 (27.27)
TKI+anti-HER2 mAB	8 (2.42)	6 (1.82)	4 (1.21)	7 (2.12)	1 (0.30)	9 (2.73)	35 (10.61)
Single TKI	17 (5.15)	17 (5.15)	7 (2.12)	7 (2.12)	7 (2.12)	15 (4.55)	70 (21.21)
Non anti-HER2	6 (1.82)	8 (2.42)	2 (0.61)	7 (2.12)	4 (1.21)	0 (0)	27 (8.18)
ADC	1 (0.30)	1 (0.30)	0 (0)	4 (1.21)	0 (0)	2 (0.61)	8 (2.42)
Total No. (%)	50 (15.15)	48 (14.55)	54 (16.36)	117 (35.45)	22 (6.67)	39 (11.82)	330 (100.00)

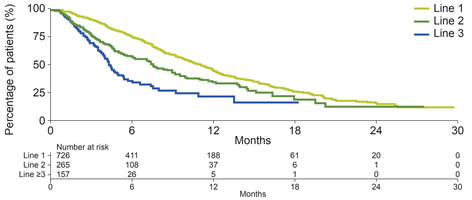
- Previous treatment history was a key factor in the choice of 1L therapy by physicians. **Figure 3** showed the distribution of 1L treatment choices
- Among the 571 patients naïve to anti-HER2 treatment, dual anti-HER2 mAB was the most common choice (42.91%, n = 245). As a comparison, of the 294 patients previously treated with anti-HER2 therapy, most (n = 116, 39.46%) opted for single TKI, followed by dual anti-HER2 mAB (n = 68, 23.13%).

Figure 3 Treatment patterns in first-line among anti-HER2 treated/naïve patients



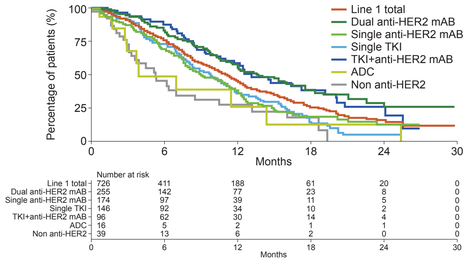
- Median real-world progression-free survival (rwPFS) of 1L and 2L treatment were 11.04 months (95% CI: 10.19-12.03) and 7.59 months (95% CI: 6.21-9.2) respectively (**Figure 4**)

Figure 4 Progression-free survival of treatment according to treatment line



- In terms of specific therapy regimen, the median rwPFS of patients treated with dual anti-HER2 mAB was 13.57 (95% CI: 12.03-17.52) months, followed by TKI+anti-HER2 mAB with a median rwPFS of 12.98 (95% CI: 11.04-20.08) months. (**Figure 5**)

Figure 5 Progression-free survival of first-line treatment according to treatment regimens



Treatment regimen	Number of patients	Progression or death, No. (%)	Censor, No. (%)	rwPFS (95% CI), month
First-line	726	385 (53.03)	341 (46.97)	11.04 (10.19, 12.03)
Dual anti-HER2 mAB	255	98 (38.43)	157 (61.57)	13.57 (12.03, 17.52)
Single anti-HER2 mAB	174	107 (61.49)	67 (38.51)	9 (7.72, 11.57)
Single TKI	146	99 (67.81)	47 (32.19)	9.83 (8.12, 11.47)
TKI+anti-HER2 mAB	96	43 (44.79)	53 (55.21)	12.98 (11.04,20.08)
Non anti-HER2	39	28 (71.79)	11 (28.21)	5.26 (3.61, 10.48)
ADC	16	10 (62.50)	6 (37.50)	3.91 (2.92, NA)

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Disclosures
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