Treatment patterns and Efficacy/Safety of the Drugs in HER2+ NSCLC: A Systemic Literature Review

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BACKGROUND[1–2]

- Lung cancer is the 2nd most common cancer in the U.S., and non-small cell lung cancer (NSCLC) consists of 85% of overall lung cancer cases.
  - About 234,580 new cases of lung cancer and 25,070 deaths are expected in 2024
- Human epidermal growth factor receptor 2 (HER2 [ErbB2]) gene mutations are found in approximately 2-5% of NSCLC cases.
- Most activating HER2 mutations in NSCLC include exon 20 insertion mutations, and these include gene mutations and amplifications in NSCLC.
- There is an unmet need to develop targeted therapies in HER2-positive (HER2+) NSCLC.

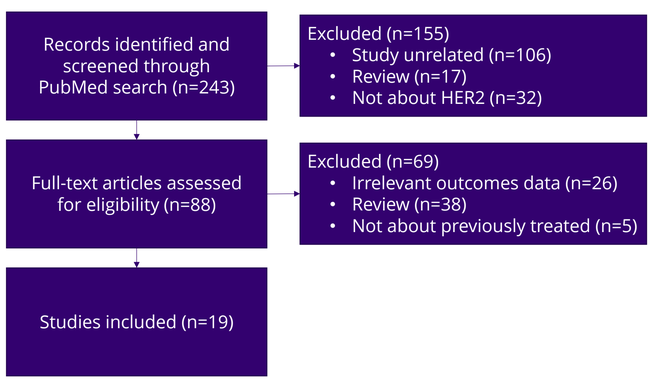
OBJECTIVE

- Identify the prior treatment patterns and assess the efficacy and safety of the studied drugs from different drug classes in patients with HER2+ NSCLC who had previously been treated with at least one anticancer regimen.

METHODS

- A systemic literature review was conducted from PubMed to analyze Phase II clinical studies focusing on patients with HER2+ NSCLC who had received at least one prior anticancer therapy.
- This review aimed to gather data on previous treatment types and outcomes of the studied drugs.
- PubMed was searched between January 2014 to August 2024 using the following key inclusion criteria:
  - Patients with HER2+ NSCLC
  - Patients who experienced progression after receiving anticancer treatment
  - Outcome measures, including ORR, PFS, mOS, and other relevant data

PRISMA DIAGRAM



RESULTS[2–20]

Table 1: List of Studied Drugs with Dosage by Each Drug Class

Drug Class	# of Studies	Studied Drugs with Dosage
Antibody Drug Conjugate (ADC)	8	• Trastzumab deruxtecan 5.4mg/kg every 3 weeks • Trastzumab deruxtecan 6.4mg/kg every 3 weeks • Ado-trastuzumab emtansine 3.6mg/kg every 3 weeks
Tyrosine Kinase Inhibitor (TKI)	7	• Poziotinib 16mg/d for 28-day cycle • Pyrotinib 400mg/d for 21-day cycle • Pyrotinib 400mg/d + Apatinib 250mg/d for 28-day cycle • Afatinib 40mg/d for 28-day cycle
Combination (Comb)	4	• Pertuzumab IV 840mg on Day 1 of Cycle 1 (every 3 weeks), then 420mg from the following cycles + Trastuzumab IV loading dose of 8mg/kg on Day 2 of Cycle 1, then 6mg/kg on Day 1 of from the following cycles + Docetaxel IV 75mg/m^2 on Day 2 of Cycle 1 and 75mg/m^2 on Day 1 from the following cycles • Loading dose of Trastuzumab 8mg/kg + Pertuzumab 840mg, then maintenance dose of Trastuzumab 6mg/kg + Pertuzumab 420mg every 3 weeks • Trastuzumab 4mg/kg, then 2mg/kg + Paclitaxel 60mg/m^2 weekly

Figure 1: Prior Treatment Patterns by Each Drug Class

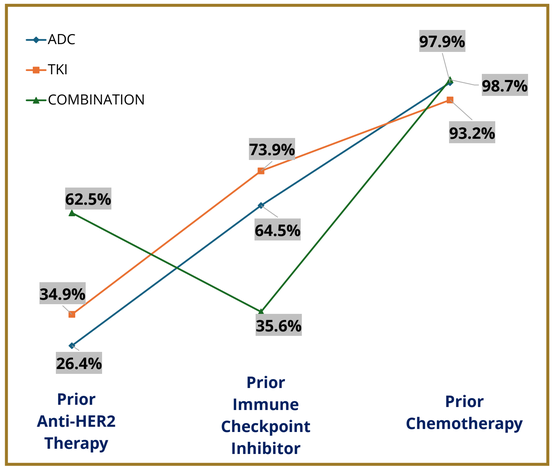


Figure 2: Efficacy Outcomes by Drug Class – DCR, ORR (90-95% CI)

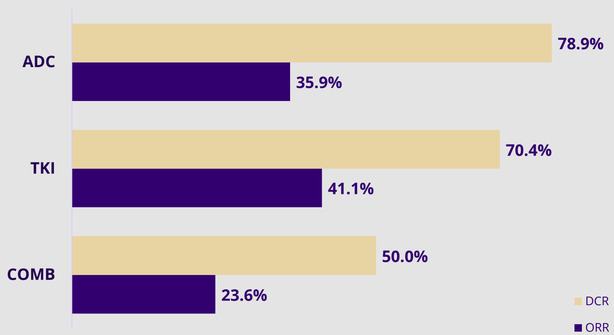


Figure 3: Efficacy Outcomes by Drug Class – mDOR, mOS, mPFS in months (90-95% CI)

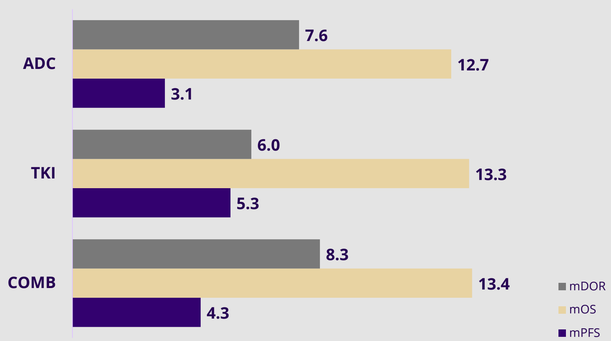
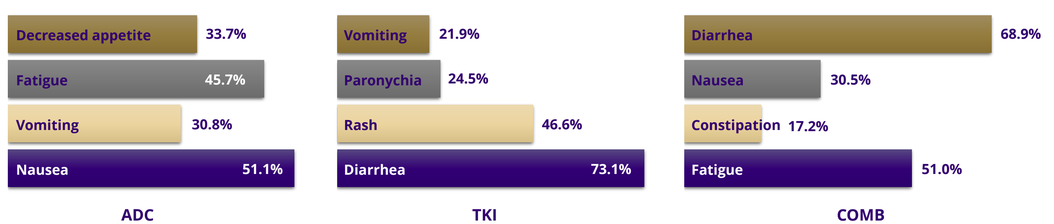


Figure 4: Adverse Events by Drug Class



Abbreviation Explanation for Figure 2 and 3:
- DCR: Disease Control Rate
- ORR: Objective Response Rate
- mDOR: Median Duration of Response
- mOS: Median Overall Survival
- mPFS: Median Progression-Free Survival

Summary of Results:
- We identified 19 Phase II clinical studies investigating the outcomes data such as DCR, ORR, mDOR, mOS, and mPFS.
  - 89.5% of studies reported ORR.
  - 63.2% of studies reported DCR.
- Median number of prior treatments among the studies was 2.15.
- Studies varied widely with:
  - Sample sizes from 13 to 105 participants.
  - Duration of treatment from 2.7 to 8.3 months.
  - Duration of follow-up from 8.6 to 17.7 months.
- Besides gastrointestinal-related side effects, some notable adverse events from TKI were paronychia and rash.

DISCUSSION

- Most (96.6%) participants had prior chemotherapy, including platinum- and non-platinum-based.
- Additionally, patients with ADC and TKI-based regimens had immune checkpoint inhibitors as their 2nd most common prior treatment.
- Treatment with ADC had the highest DCR.
- Treatment with TKI had the highest ORR.
- All treatment classes had similar mOS. mDOR and mPFS were different by approximately one month for each class.
- Majority of adverse events from all drug classes were related to gastrointestinal disorders.
- Further studies should continue to explore the standard of care in patients with HER2+ NSCLC after progressing on more than one line of therapy.

References

Questions?
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