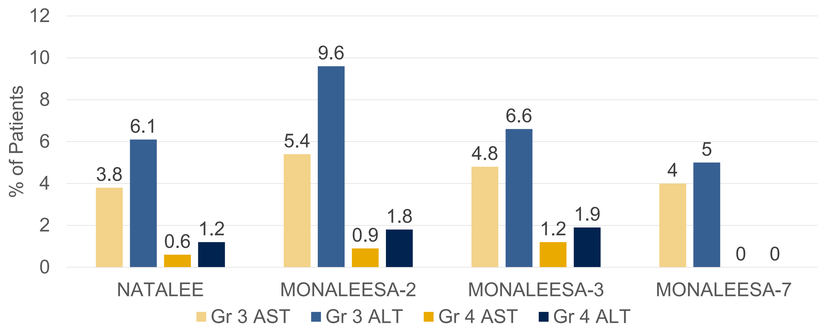
Real-World Evaluation of Hepatotoxicity During Treatment with Ribociclib

Jordan Hill, PharmD, BCOP, Brooke Kielkowski, PharmD, Stephanie Nolfi, APRN, AOCNP,
Christinea Marino, AOCNP, CBCN, Lindsay Thomas, PA-C
West Virginia University Cancer Institute
Morgantown, West Virginia

Background

- Ribociclib is widely used in HR+/HER2- breast cancer as it has demonstrated improvement in EFS, PFS, and OS in multiple phase III clinical trials including NATALEE and MONALEESA-2, 3, and 7.[1-4]
- Hepatotoxicity has emerged as a notable adverse reaction with the incidence ranging from 4-10% for grade 3 and 0-2% for grade 4.



- The mechanism of ribociclib-induced hepatotoxicity remains unclear but may involve direct hepatocyte toxicity, mitochondrial dysfunction, or immune-mediated mechanisms.
- Given the potentially serious nature of hepatotoxicity and its impact on treatment adherence and outcomes, it is critical to understand its real-world incidence.
- This study aims to evaluate the incidence of hepatotoxicity in patients receiving ribociclib within our cancer institute compared to rates reported in previous clinical trials.

Objectives

- **Primary**
  - Compare the incidence of grade 3-4 hepatotoxicity in patients with HR+/HER2- breast cancer treated with ribociclib in combination with endocrine therapy at our institution to previously reported rates in pivotal trials
- **Secondary**
  - Assess the median time to onset and resolution of hepatotoxicity
  - Evaluate the outcomes of therapy interruptions, dose reductions, and re-challenge of ribociclib
  - Identify baseline characteristics with the potential to predispose patients to ribociclib-induced hepatotoxicity

Methods

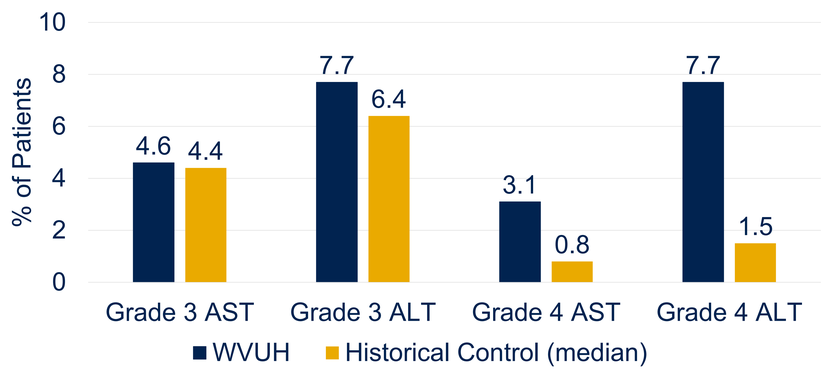
- **Design:** Retrospective chart review
- **Inclusion criteria:** Patients treated with ribociclib at WVU Medicine between March 2017 and March 2025
- **Exclusion criteria:** Patients who received fewer than 14 days of treatment (n=25) were excluded
- Liver function test abnormalities during treatment were assessed and graded according to CTCAE v5.0 criteria
- Data on baseline liver disease, liver metastases, concurrent hepatotoxic medications, and CYP3A4 inhibitors were collected

Results

Table 1. Baseline Characteristics

Patient Characteristic	Total (N=65)	Gr 2-4 LFTs (n=14)
Median age, years	60	52
Female, n (%)	64 (98)	14 (100)
Cancer stage, n (%) - Stage II-III - Stage IV	 22 (34) 43 (66)	 4 (29) 10 (71)
Initial dose of 600 mg, n (%)	42 (65)	10 (71)
Pre-existing liver disease, n (%)	12 (18)	1 (7)
Liver metastases, n (%)	7 (11)	2 (14)

Figure 1. Incidence and Severity of Hepatotoxicity



Results

Table 2. Adverse Event Characteristics and Management

Hepatotoxicity Characteristics	
Median onset, weeks (range)	15 (2-29)
Treatment held at development of G2-4 toxicity, n (%)	14 (100)
Median time to recovery, weeks (range)	11 (4-30)
Recurrent hepatotoxicity upon rechallenge, n (%)	3 (100)
Concomitant CYP3A4 inhibitors or hepatotoxic agents, n (%)	0 (0)

Discussion

- Majority of patients were stage IV and initiated on 600 mg with very few patients having liver metastasis or underlying liver disease.
- Limited data exists regarding hepatotoxicity during treatment with ribociclib in the real-world setting. Prior real-world evidence from Bas, et al. and Nawaz, et al. showed similar rates of hepatotoxicity to published literature, different than what was found at our institution.[5,6]
- No prior real-world data evaluated baseline characteristics with the potential to predispose patients to hepatotoxicity.
- Limitations of this study include the retrospective nature, small number of patients, and inclusion of patients receiving more than 14 days of therapy but a shorter duration than the median onset for hepatotoxicity.

Conclusion

- In this real-world cohort, the incidence of grade 4 hepatotoxicity with ribociclib was significantly higher than reported in clinical trials, underscoring the importance of vigilant hepatic monitoring.
- Hepatotoxicity occurred independently of baseline liver metastases, pre-existing liver disease, or concurrent use of hepatotoxic agents.
- Rechallenge following grade 3 hepatotoxicity was associated with recurrence, suggesting cautious consideration before re-initiation.
- These findings highlight the need for personalized risk assessment and further investigation into predictors of severe hepatotoxicity in patients treated with ribociclib.

References

1. Slamon DJ, Lipatov O, Nowecki Z, et al. N Engl J Med 2024;390(12):1080-1091.
2. Hortobagyi GN, Stemmer SM, Burris HA, et al. N Engl J Med 2022;386(10):942-950.
3. Slamon DJ, Neven P, Chia S, et al. J Clin Oncol 2018;36:2465-2472.
4. Lu YS, Im SA, Colleoni M, et al. Clin Canc Res 2022;28(5):851-859.
5. Bas O, Inci BK, Eroglu I, et al. Ann Oncol 2024;35(2):S1099.
6. Nawaz A, Zekri J, Rasool HJ. J Clin Oncol 39, 2021 (suppl 15; abstr e13024).

Disclosure: Authors have no conflicts of interest to disclose.