SKIPPirr: Evaluating Prophylactic Strategies to Reduce the Incidence of Infusion-related Reactions (IRRs) With Amivantamab

Rationale

- In CHRYSALIS, a phase 1 study, intravenous (IV) amivantamab has an IRR incidence of ~67% at first infusion[1,a]
- Standard mitigation approaches in clinical trials include a **split first dose of amivantamab over 2 days in the first cycle** and premedication with oral or IV antihistamines, oral or IV antipyretics, and IV glucocorticoids[1,2]

SKIPPirr Study Design

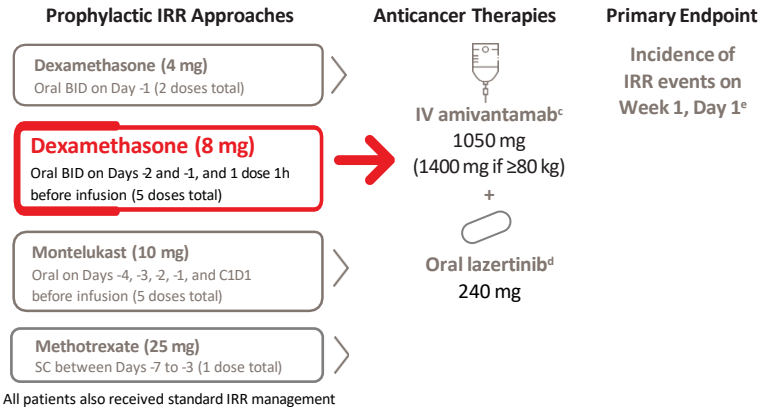
SKIPPirr was a phase 2 prospective study (NCT05663866) that assessed prophylactic strategies administered prior to amivantamab infusion in order to reduce the incidence and/or severity of first-dose IRRs. This Simon's 2-stage study design evaluated prophylactic approaches in 4 cohorts, with the dexamethasone 8 mg oral cohort reaching the expansion stage.[b]

Limitation:

- The dexamethasone 8 mg oral cohort sample size is n=40

Key Eligibility Criteria

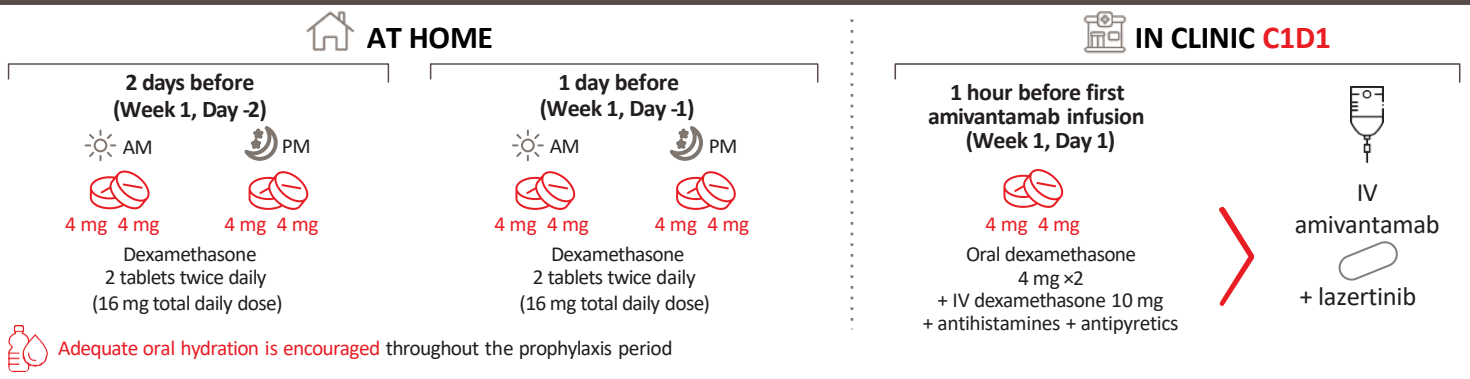
- *EGFR* Ex19del or L858R advanced/metastatic NSCLC
- Progression on or after prior treatment with osimertinib and platinum-based chemotherapy
- ECOG PS 0–1



All patients also received standard IRR management

One cohort tested in SKIPPirr reached the expansion stage: oral dexamethasone 8 mg cohort[3]

Prophylactic schedule



Adequate oral hydration is encouraged throughout the prophylaxis period

In SKIPPirr, the Week 1, Day 1 IV dexamethasone dose is 10 mg. In the amivantamab Prescribing Information, the Week 1, Day 1 IV dexamethasone dose is 20 mg.[2,3]

Rate of IRRs on C1D1

67.4%
Standard IRR management[1,f]
(historic; 256/380)

22.5%
Dexamethasone 8mg IRR prophylaxis regimen cohort
(9/40)

No grade ≥3 IRRs with dexamethasone 8 mg prophylaxis vs **2%** with standard IRR management

- **~3-fold reduction** in rate of IRRs compared with historical data[1]
- **No grade ≥3 IRRs** observed. All symptoms were grade 1 to 2
- Most common IRR-related symptoms were nausea (8%), dyspnea (5%), and hypotension (5%)

SKIPPirr is not a comparative study. Please refer to the full publication for additional information.

Administration time of amivantamab IV infusion on C1D1[g]

Standard IRR management[1,f]

5.0 h

Dexamethasone 8mg IRR prophylaxis regimen cohort

4.4 h

[a]Based on an analysis of the CHRYSALIS study.
[b]Stage 1: n=6. Stage 2: n=16. Expansion stage: n=40. See full publication for more details.
[c]IV amivantamab: 1050 mg (1400 if ≥80 kg) once weekly for 4 weeks and then every 2 weeks thereafter.
[d]Administer lazertinib any time prior to amivantamab when given on the same day.
[e]Defined as IRR events with onset within 24 hours of the start of the C1D1 amivantamab infusion and prior to the start of the C1D2 infusion.
[f]Standard IRR management included premedication with antihistamines, antipyretics, and glucocorticoids.
[g] By C1D15 and onward, the median duration of amivantamab infusion was approximately 2.3 hours for all cohorts.

BID, twice daily; C1D1, Cycle 1, Day 1; C1D2, Cycle 1, Day 2; C1D15, Cycle 1, Day 15; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; h, hour; IRR, infusion-related reaction; IV, intravenous; NSCLC, non-small cell lung cancer; SC, subcutaneous.

1. Park K, et al. *Lung Cancer*. 2023;178:166–171. **2.** RYBREVANT® (amivantamab-vmjw) [prescribing information]. Janssen Biotech, Inc.; 2025.
3. Spira AI, et al. *J Thor Oncol*. 2025:S1556-0864(25)00051-6.

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