SKIPPirr

Preventing Infusion-related Reactions With Intravenous Amivantamab: Primary Results From SKIPPirr, a Phase 2 Study

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Introduction

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- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1–3]
- In the US, IV amivantamab is now:
  - Approved for 1L treatment of patients with *EGFR*-mutated NSCLC in combination with lazertinib (MARIPOSA)[4,5]
  - Pending approval for 2L treatment of patients with *EGFR*-mutated NSCLC after osimertinib, in combination with chemotherapy (MARIPOSA-2)[6]
  - Approved for 1L treatment of patients with *EGFR* Exon20ins+ NSCLC in combination with chemotherapy (PAPILLON)[5,7]
- IV amivantamab has an IRR incidence of ~67% at first infusion[8]
  - Mitigation approaches in the clinical trials included splitting the first dose over 2 days and premedicating with antihistamines, antipyretics, and glucocorticoids

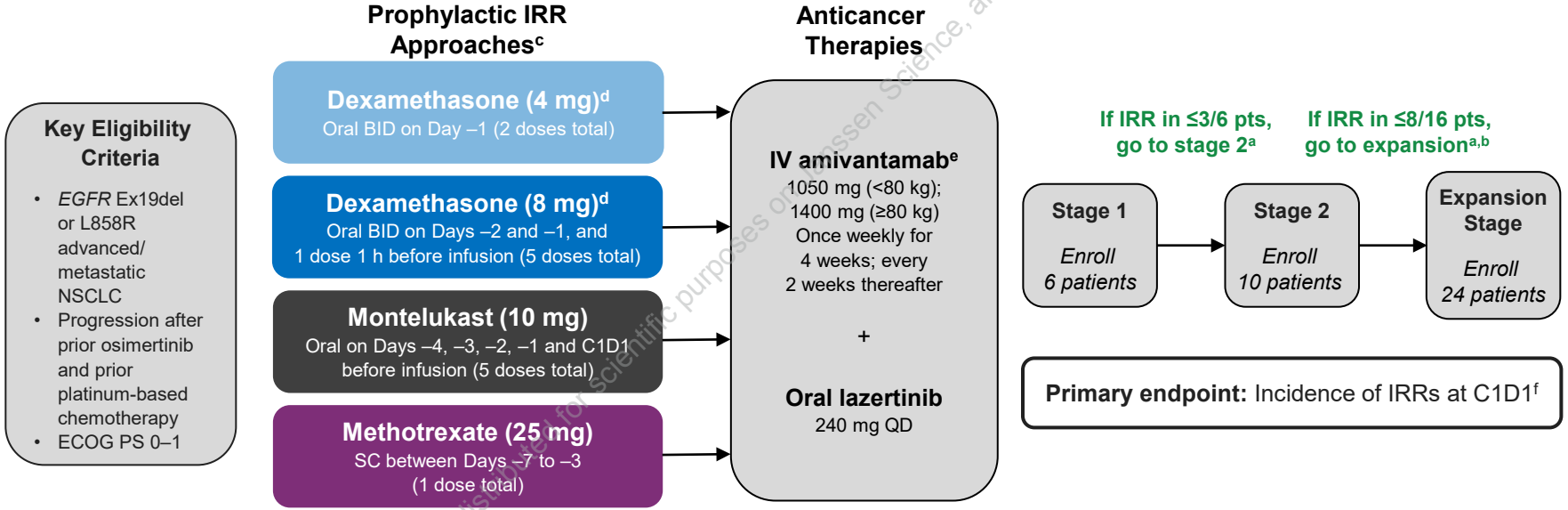
SKIPPirr evaluated additional prophylactic strategies to reduce the incidence of IRRs with IV amivantamab

1L, first-line; 2L, second-line; EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; IV, intravenous.

1. Moores SL, et al. *Cancer Res.* 2016;76(13):3942–3953. 2. Vijayaraghavan S, et al. *Mol Cancer Ther.* 2020;19(10):2044–2056. 3. Yun J, et al. *Cancer Discov.* 2020;10(8):1194–1209. 4. Cho BC, et al. *N Engl J Med.* 2024. doi:10.1056/NEJMoa2403614. 5. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 6. Passaro A, et al. *Ann Oncol.* 2024;35(1):77–90. 7. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039–2051. 8. Park K, et al. *Lung Cancer.* 2023;178:166–171.

SKIPPirr Phase 2 Study Design

- A Simon's 2-stage design[a] with an expansion stage[b] was used to evaluate 4 independent prophylactic strategies
- Median age was 63.5 years, 65% were female, and 62% were Asian, with a median of 3 prior therapy lines



SKIPPirr (ClinicalTrials.gov Identifier: NCT05663866). [a]Stage 1 was stopped if the number of patients with IRR was ≥4 (out of 6). The null hypothesis was rejected if the number of patients with IRR was ≤8 (out of 16), and the cohort was declared promising in lowering IRRs. [b]The cohort proceeded to the expansion stage if the Simon's 2-stage design was positive. [c]Patients were sequentially enrolled into prophylactic regimens. [d]If both cohorts had positive results, only 1 moved on to stage 2 as determined by the SET. [e]Patients in all cohorts also received standard premedication with antihistamines, antipyretics, and glucocorticoids. [f]IRR on C1D1 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.

BID, twice daily; C, Cycle; D, Day; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; IRR, infusion-related reaction; IV, intravenous; NSCLC, non-small cell lung cancer; QD, once daily; pts, patients; SC, subcutaneous; SET, study evaluation team.

Simon 2-stage Results

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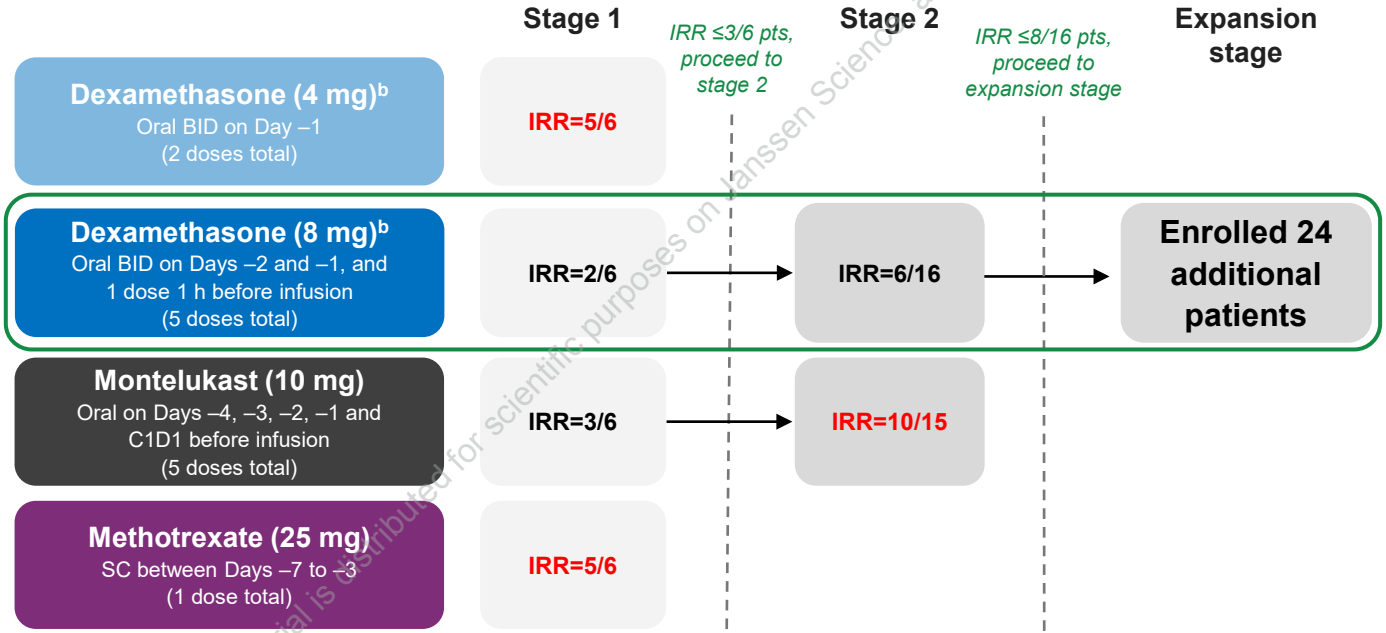
- 4 mg dexamethasone and 25 mg methotrexate prophylactic approaches did not pass stage 1; montelukast did not pass stage 2
- Only prophylaxis with dexamethasone 8 mg passed both stages and proceeded to the expansion stage



Clinical cutoff: C1D2. [a]IRR on C1D1 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. [b]If both cohorts have positive results, only 1 will move on to stage 2 as determined by the SET.
BID, twice daily; C, Cycle; CI, confidence interval; D, Day; IRR, infusion-related reaction; pts, patients; SC, subcutaneous; SET, study evaluation team.

Dexamethasone 8 mg oral prophylaxis reduced the rate of IRRs[a]

Prophylaxis with dexamethasone reduced the amivantamab IRR rate to 22.5%

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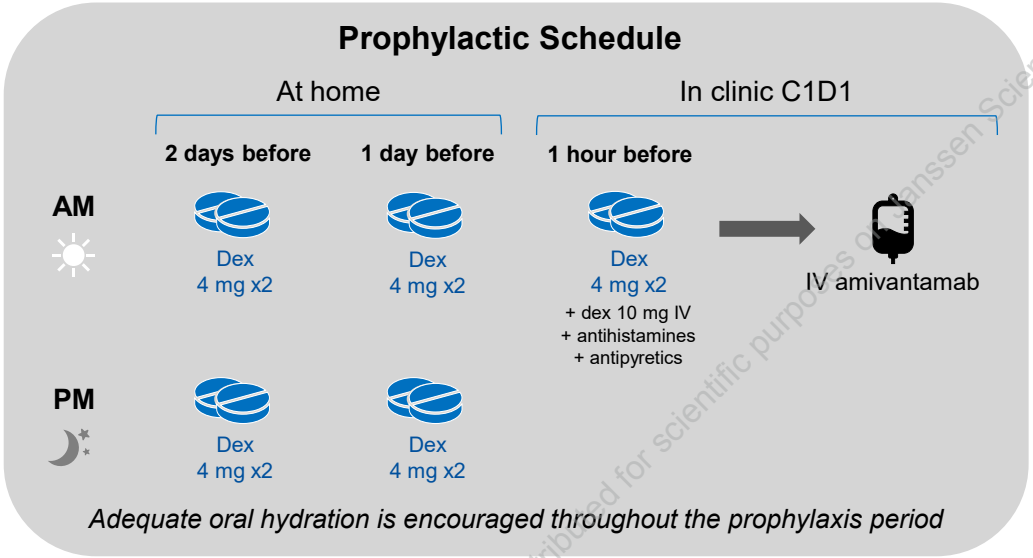

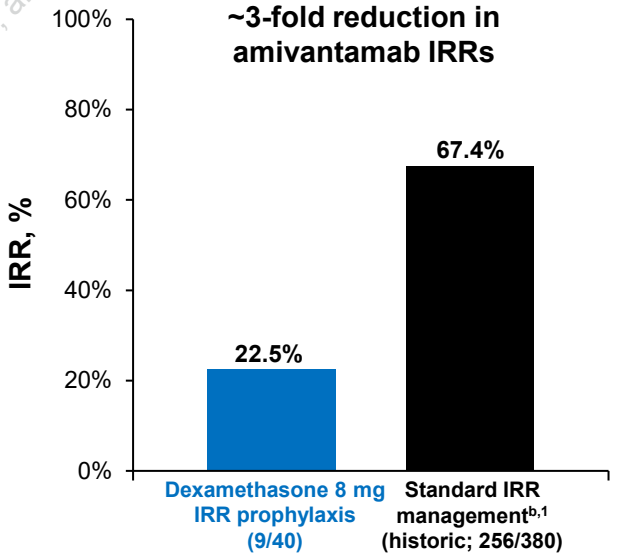

Clinical cutoff: C1D2. [a]IRR on C1D1 defined as IRR events with onset within 24 hours of the start of the C1D1 amivantamab infusion and prior to the start of the C1D2 infusion. [b]Includes standard premedications (antihistamines, antipyretics, and glucocorticoids).

BID, twice daily; C, Cycle; D, Day; dex, dexamethasone; IRR, infusion-related reaction; IV, intravenous.

1. Park K, et al. *Lung Cancer*. 2023;178:166–171.

Incidence of IRRs and IRR-related Symptoms on C1D1

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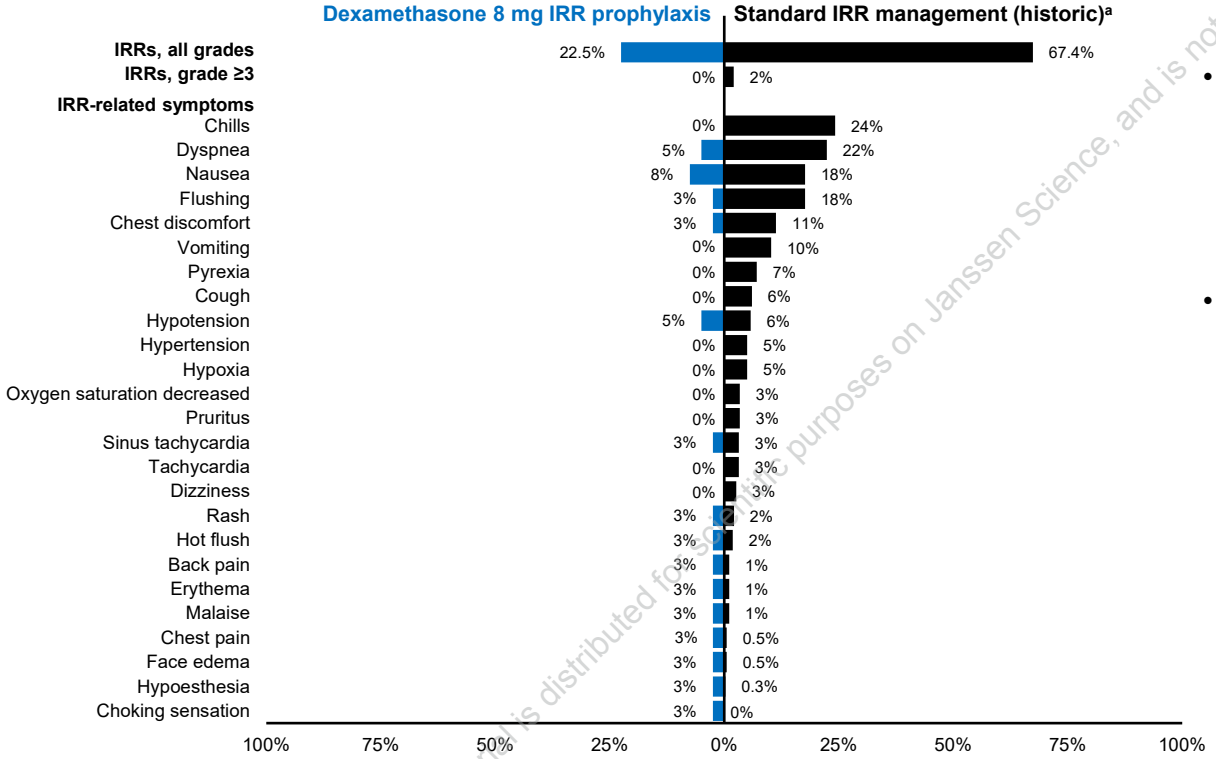

- On C1D1, the IRR rate was 22.5% (95% CI, 10.8–38.5) for patients receiving dexamethasone 8 mg prophylaxis
  - IRRs were grade 1–2 (no grade ≥3)
  - No IRR SAEs
- The most common IRR-related symptoms were nausea (8%), dyspnea (5%), and hypotension (5%)
  - All symptoms were grade 1–2 (no grade ≥3)

[a]IRR symptoms on C1D1 with IV amivantamab monotherapy are reported in the 380 patients treated at the RP2D in the CHRYSALIS study based on a March 30, 2021 data cutoff. Includes standard premedications (antihistamines, antipyretics, and glucocorticoids).

BID, twice daily; C, Cycle; CI, confidence interval; D, Day; IRR, infusion-related reaction; IV, intravenous; RP2D, recommended phase 2 dose; SAE, serious adverse event.

Conclusions

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- Prophylactic treatment with dexamethasone 8 mg oral BID on C1D–2, C1D–1, and 1 hour prior to infusion on C1D1 (5 doses total)[a] resulted in a ~3-fold reduction in IRR incidence (from 67.4% to 22.5%) compared with standard IRR management[a]
- Patients receiving dexamethasone 8 mg experienced fewer IRR-related symptoms (no grade ≥3)
  - Most common symptoms were nausea, dyspnea, and hypotension
- No new safety signals were observed

Dexamethasone 8 mg oral BID prophylaxis is an effective strategy to reduce IRRs with IV amivantamab

[a]Includes standard premedications (antihistamines, antipyretics, and glucocorticoids).
BID, twice daily; C, Cycle; D, Day; IRR, infusion-related reaction; IV, intravenous.

Other Amivantamab Presentations at WCLC 2024

MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am
(OA02.03; Gadgeel)

MARIPOSA

Patient-relevant outcomes of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Tuesday, Sep 10 1:55-2:00pm
(MA12.07; Nguyen)

MARIPOSA

Lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 11:07-11:17am
(OA02.05; Lee)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am
(OA09.05; Alexander)

PAPILLON

High-risk biomarker subpopulations from patients with *EGFR* Ex20ins in PAPILLON

Tuesday, Sep 10 1:50-1:55pm
(MA12.06; Goldman)

EGFR esisters

Development of a **patient-friendly lung cancer lexicon**:
Sunday, Sep 8 6:15-7:45pm
(P2.16F.03; Feldman)

Poster tour: Monday, Sep 9 6:45-6:53pm

Additional posters:

- **COCOON TiP:** Enhanced vs standard dermatologic management with amivantamab + lazertinib in advanced NSCLC**:** Monday, Sep 9 12:00-2:00pm (P3.12D.04; Cho)
- **PolyDamas TiP:** Amivantamab + cetrelimab in advanced NSCLC: Virtual ePoster (EP.12H.02; Voon)
- 5-year survival estimates with 1L osimertinib for *EGFR*-mutant advanced NSCLC in the US: Virtual ePoster (EP.12A.03; Sabari)

Acknowledgments

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