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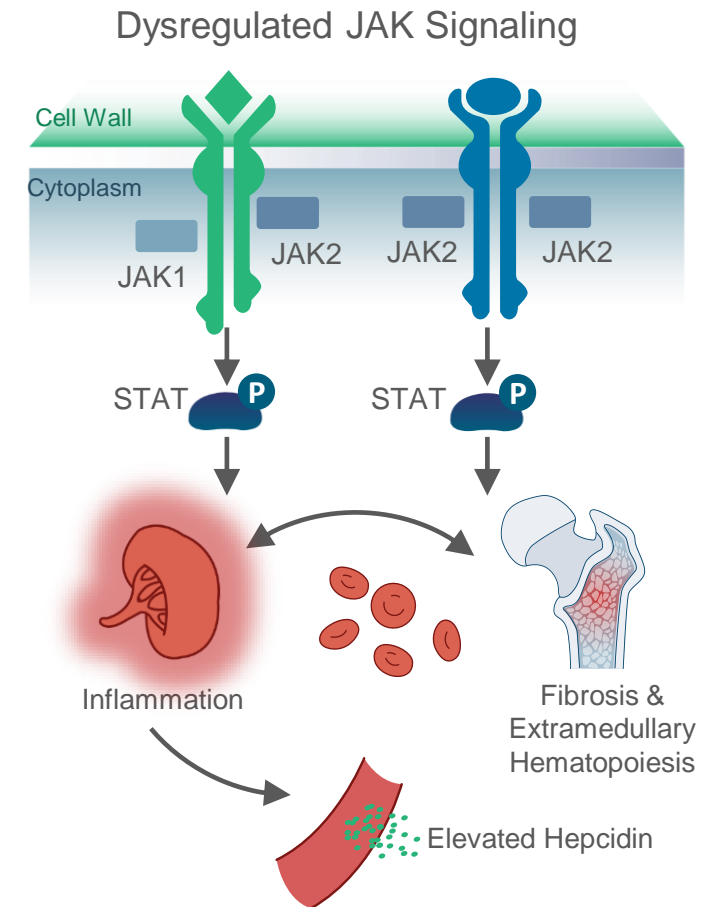
# Robust Overall Survival and Sustained Efficacy Outcomes During Long Term Exposure to Momelotinib in JAK Inhibitor Naïve and Previously JAK Inhibitor Treated Intermediate/High Risk Myelofibrosis Patients

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# Background: Myelofibrosis (MF)

- **Dysregulated JAK-STAT signaling**
  - Progressive anemia, splenomegaly and constitutional symptoms
- **Approved JAK inhibitors**
  - Ruxolitinib and fedratinib
  - Intrinsically myelosuppressive
  - Dose dictated by platelet count
- **OS advantage with ruxolitinib**
  - Short OS following JAK inhibitor discontinuation



# Background: Momelotinib (MMB)

## Momelotinib (MMB) is a JAK1, JAK2 and ACVR1 inhibitor

- Ph3 MOMENTUM trial ongoing
- Previous Ph3 studies: SIMPLIFY-1 and SIMPLIFY-2
  - In JAK inhibitor naïve (S1) and JAK inhibitor treated (S2) patient populations
- **Previously reported data suggests that momelotinib:**
  - Provides similar splenic response for momelotinib vs ruxolitinib
  - Improves constitutional symptoms
  - Reduces transfusion burden and improves anemia
  - Has a favorable safety profile

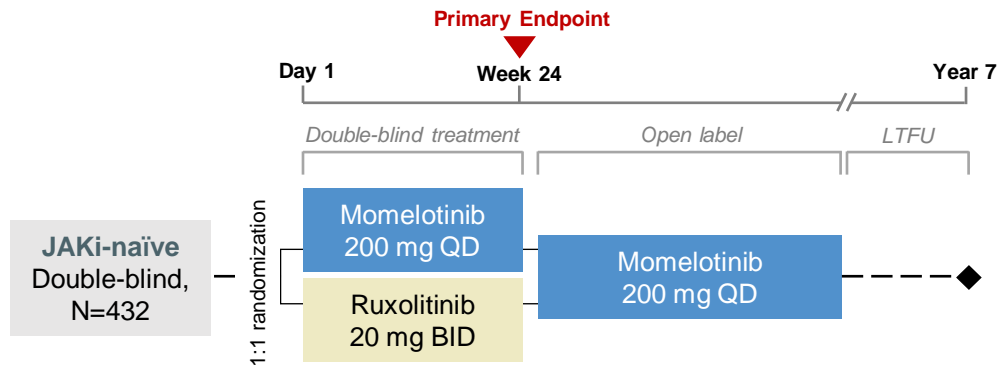
## SIMPLIFY-1

|                                  | Safety Population<br>(Randomized Period) |                |
|----------------------------------|--|----------------|
|                                  | MMB<br>(N=214)                           | RUX<br>(N=216) |
| Subjects with any Grade 3/4 TEAE | 74 (34.6%)                               | 94 (43.5%)     |
| Thrombocytopenia Grade 3/4       | 15 (7.0%)                                | 10 (4.6%)      |
| Anemia Grade 3/4                 | 13 (6.1%)                                | 49 (22.7%)     |

# Background: Completed Phase 3 Studies SIMPLIFY-1 and 2

## SIMPLIFY-1: 1<sup>st</sup>-Line Population

JAK inhibitor naïve



**Goal:** Non-Inferiority

**MMB:** N=215

**RUX:** N=217

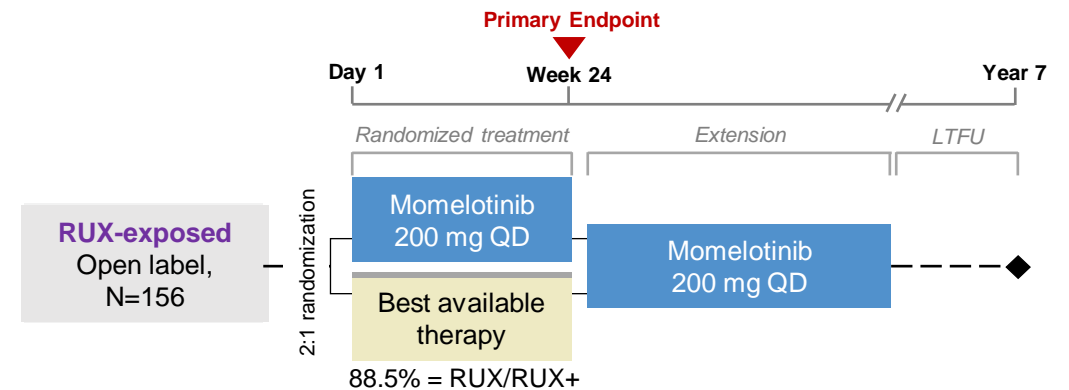
**Primary Endpoint** Splenic Response Rate

**Secondary Endpoints**

- Total Symptom Score
- Transfusion Independence Rate

## SIMPLIFY-2: 2<sup>nd</sup>-Line Population

Prior ruxolitinib with anemia or thrombocytopenia



**Goal:** Superiority

**MMB:** N=104

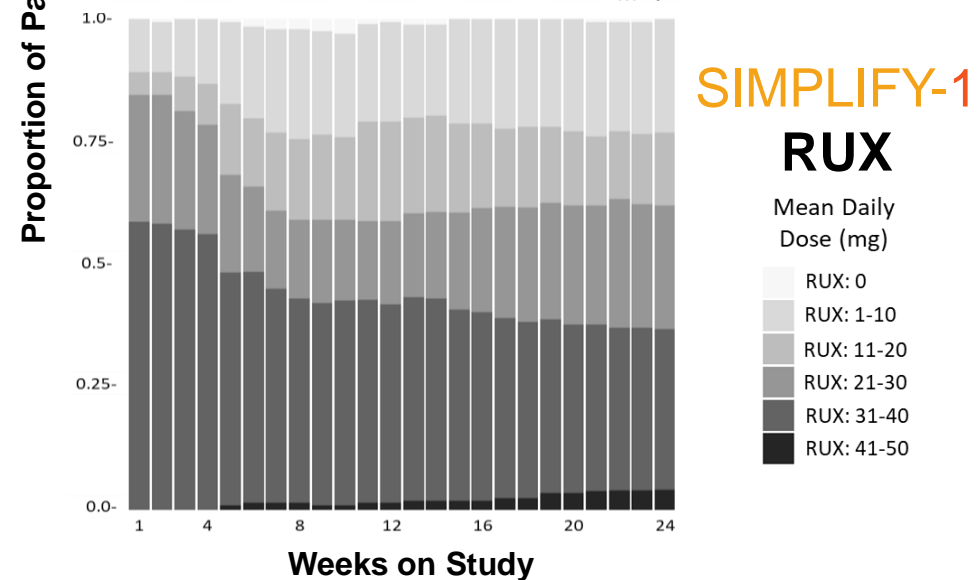
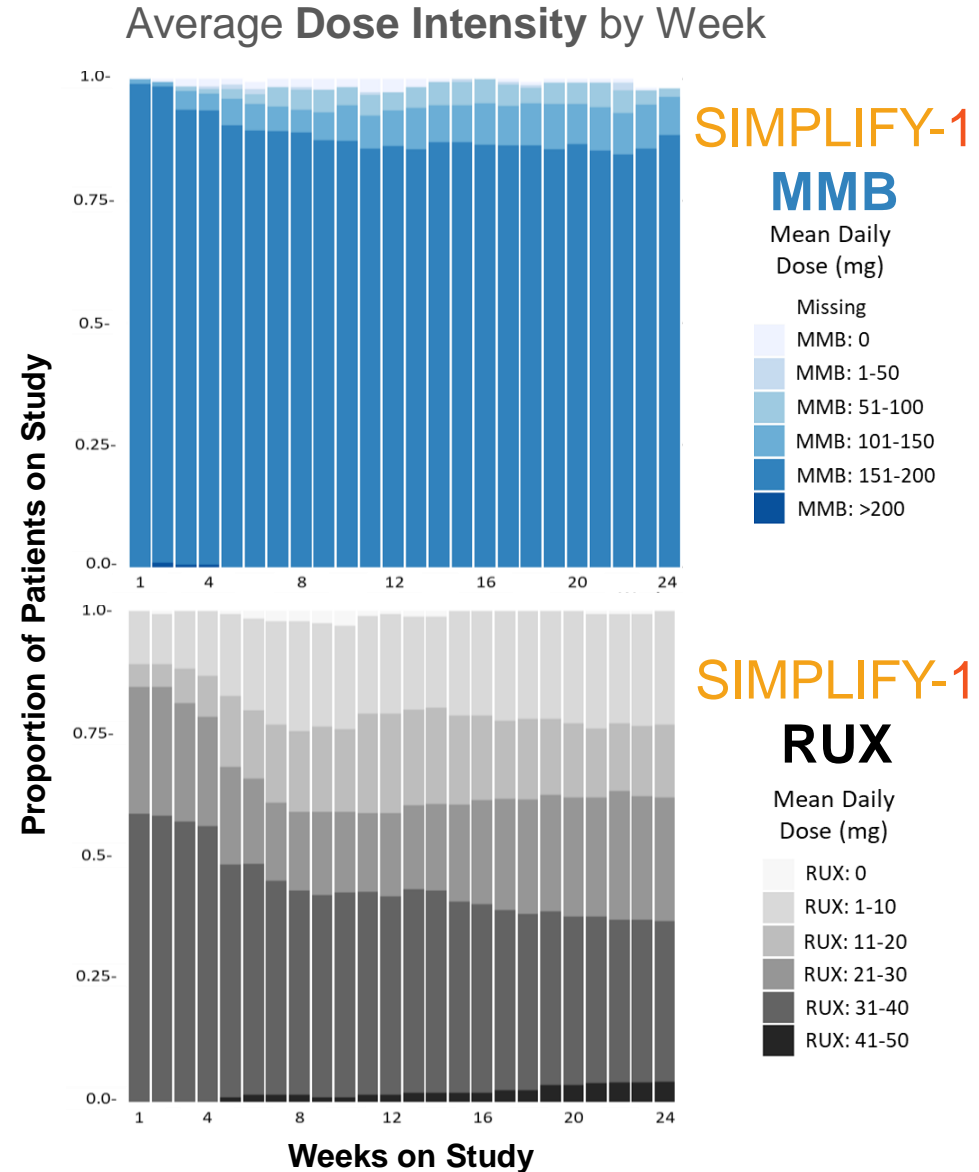
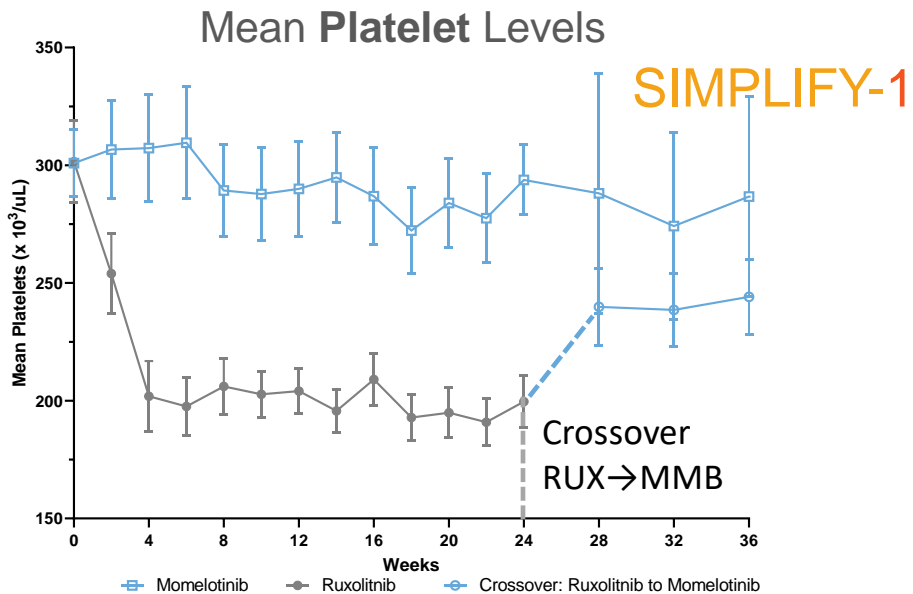
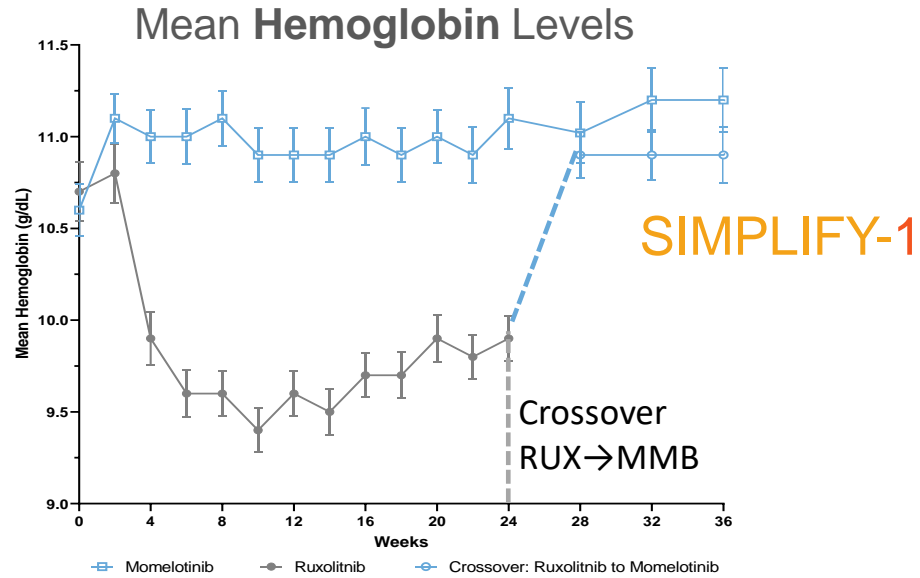
**BAT:** N=52

**Primary Endpoint** Splenic Response Rate

**Secondary Endpoints**

- Total Symptom Score
- Transfusion Independence Rate

# Momelotinib: Differentiated Heme Profile Allows High Dose Intensity

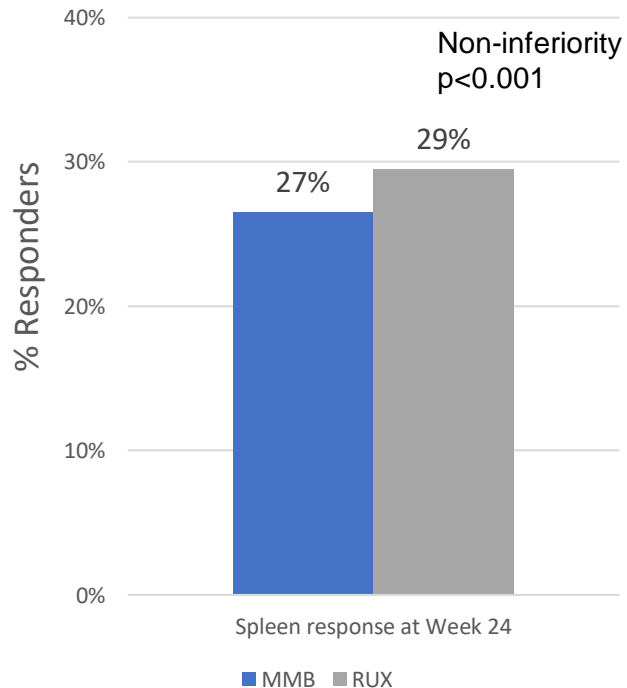


# SIMPLIFY-1: Splenic Response and Duration of Splenic Response

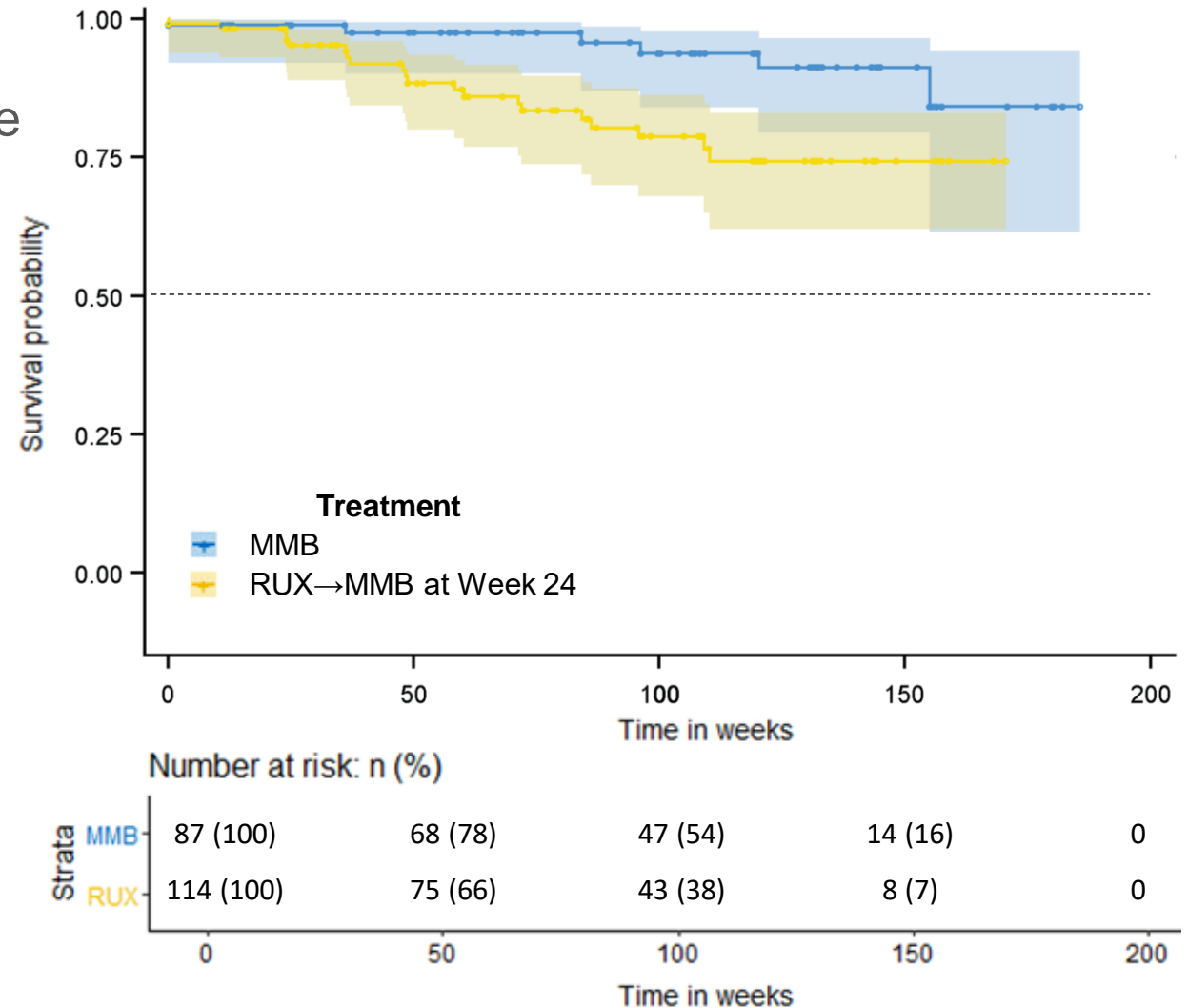
- 40% of patients on MMB achieved a splenic response at any time
- Duration measured from  $\geq 35\%$  reduction from baseline to return to baseline volume

## SIMPLIFY-1

### Week 24 Splenic Response Rate



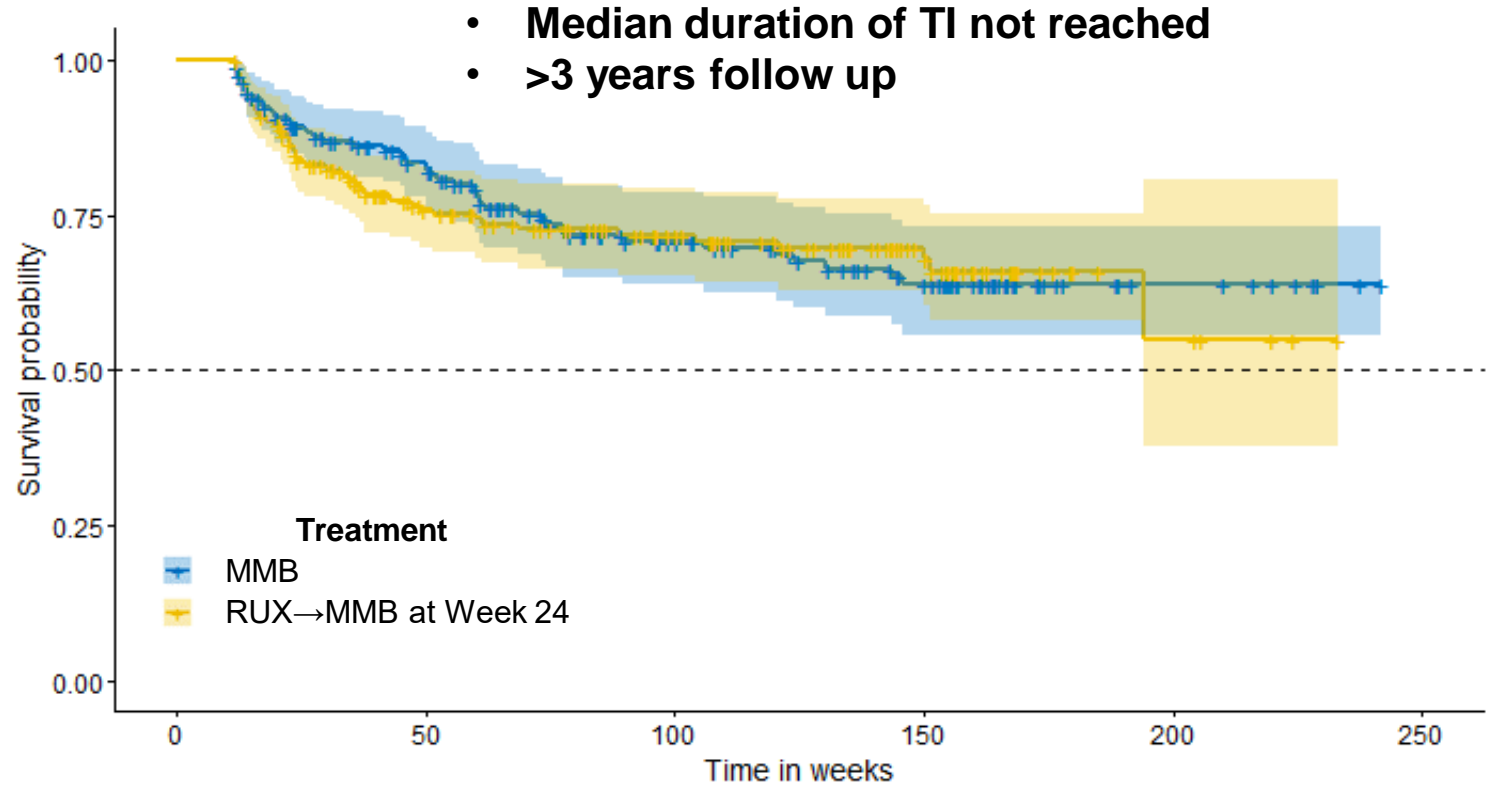
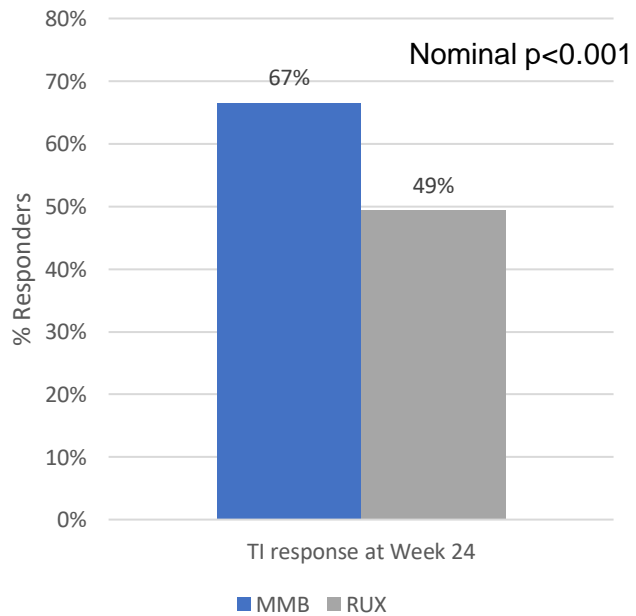
### Median Duration of Splenic Response Not Reached on MMB



# SIMPLIFY-1: Transfusion Independence and Duration of TI

## SIMPLIFY-1

Landmark Week 24 TI Rate



Number at risk: n (%)

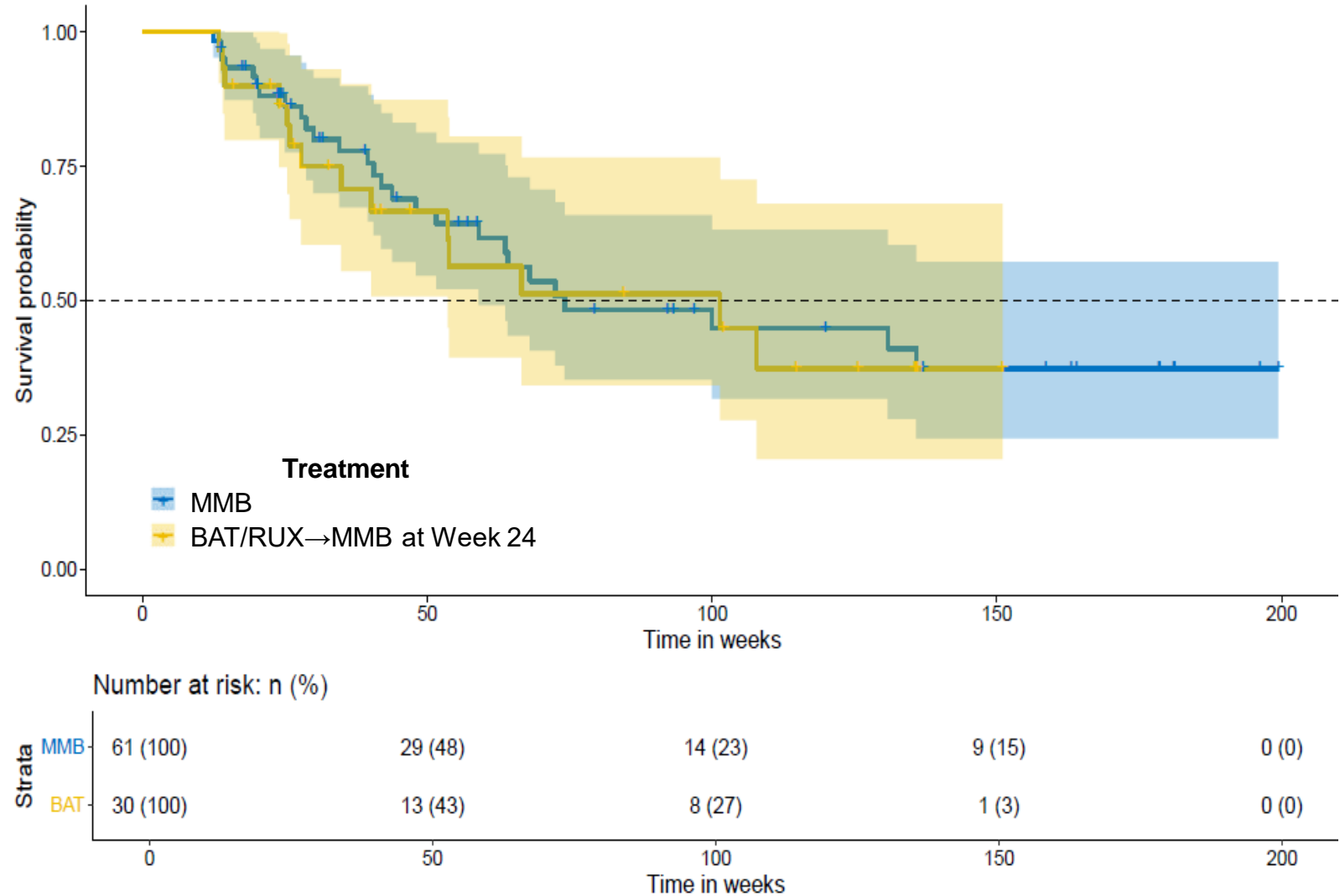
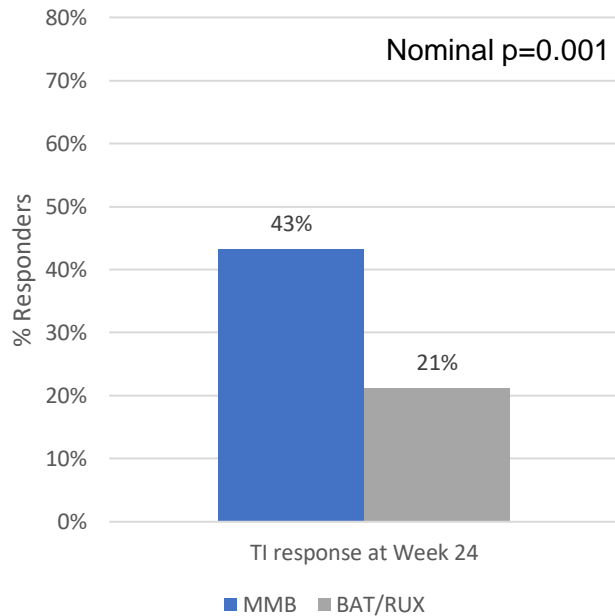
| Strata | 0         | 50       | 100     | 150     | 200   | 250   |
|--------|-----------|----------|---------|---------|-------|-------|
| MMB    | 177 (100) | 119 (67) | 71 (40) | 46 (26) | 9 (5) | 0 (0) |
| RUX    | 182 (100) | 101 (55) | 74 (41) | 39 (21) | 5 (3) | 0 (0) |

Time in weeks

# SIMPLIFY-2: Transfusion Independence and Duration of TI

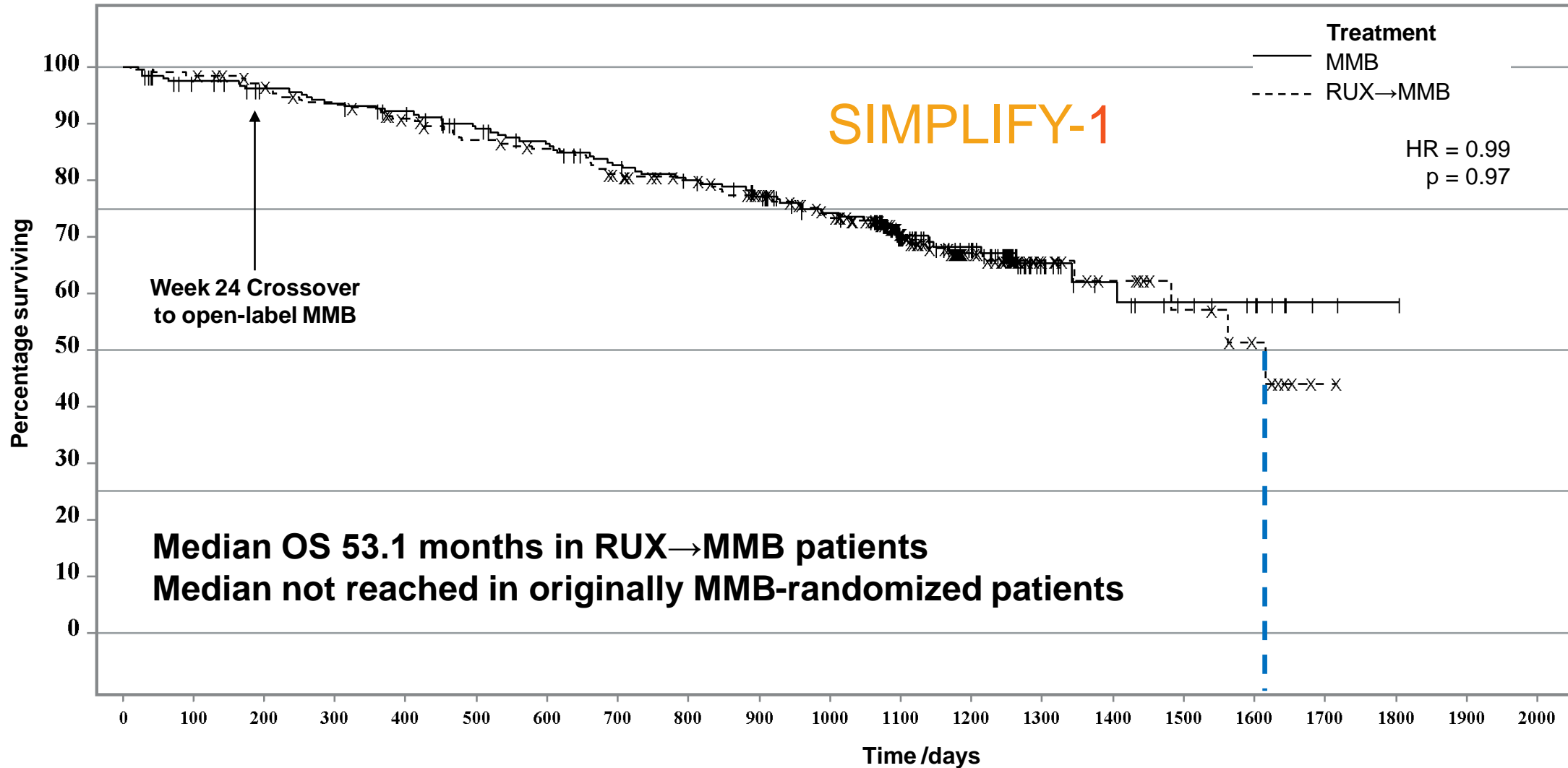
## SIMPLIFY-2

Landmark Week 24 TI Rate

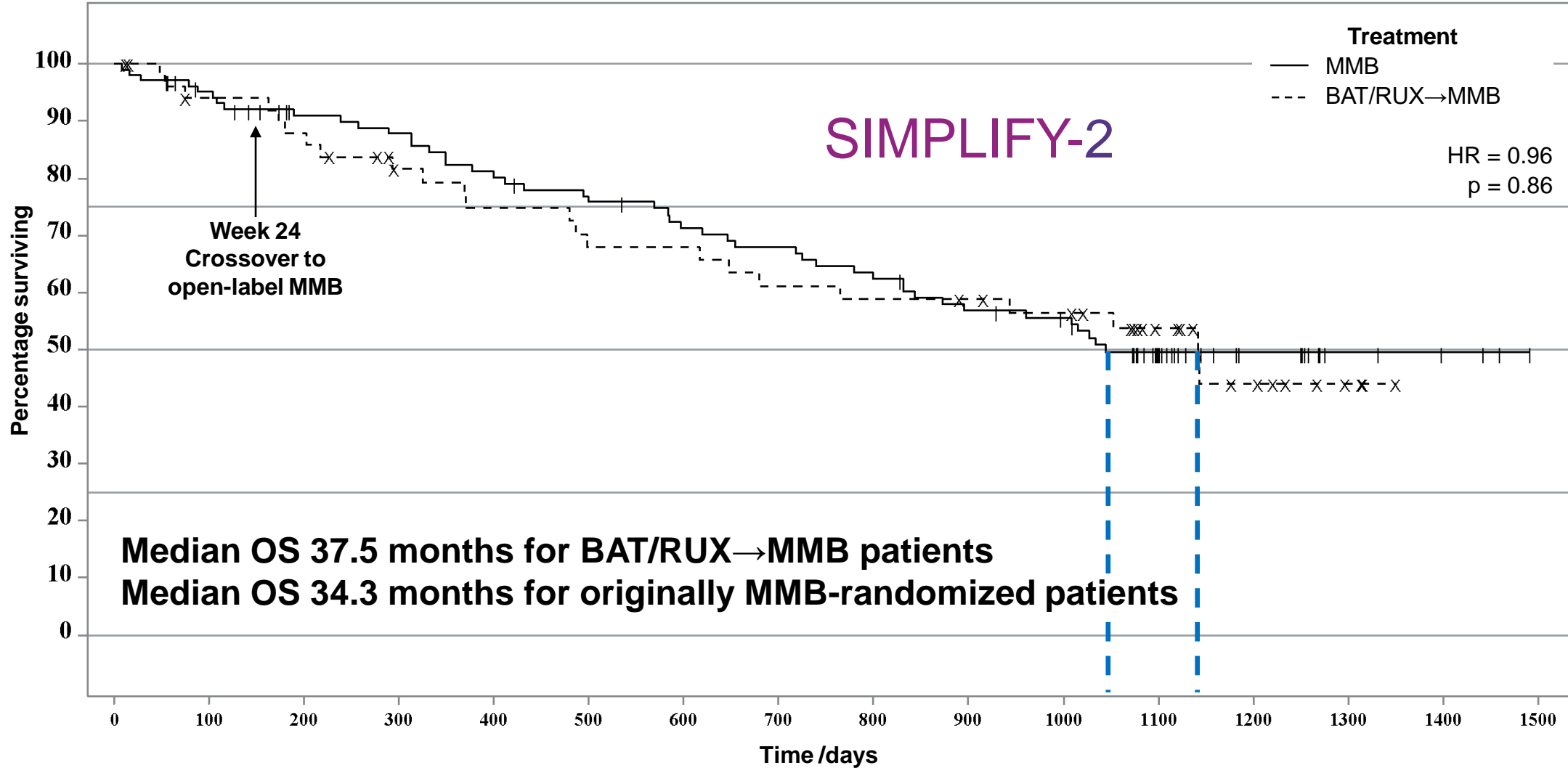




# SIMPLIFY-1: Robust Survival for JAKi-naïve Patients



# SIMPLIFY-2: Robust Survival for Prior-JAKi Treated Patients



# Conclusions

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- Robust OS in both JAKi-naïve and previously ruxolitinib treated patients
  - SIMPLIFY-1 mOS (53.1 m and not reached) consistent with OS advantage in MF provided by JAK inhibition
  - SIMPLIFY-2 mOS (34.3 and 37.5 m) represent the best reported OS in this previously ruxolitinib-treated setting
- Sustained transfusion independence and splenic response observed
- The durability of activity and survival data are consistent with momelotinib's clinical and biologic profile:
  - JAK1, JAK2, ACVR1 inhibition
  - Potential to improve splenomegaly, constitutional symptoms and anemia
  - Low myelosuppressive potential and lack of cumulative toxicity

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