

Renal events and peripheral neuropathy reported with momelotinib in myelofibrosis: an indication-restricted FAERS study

Jia Luo

lawga666@163.com

The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangdong Clinical Research Academy of Chinese Medicine

Hongxuan Cao

Guangzhou University of Chinese Medicine, University of Chinese Medicine

Research Article

Keywords: momelotinib, myelofibrosis, FAERS, pharmacovigilance, renal adverse events, peripheral neuropathy

Posted Date: October 20th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11425485/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Renal events and peripheral neuropathy reported with momelotinib in myelofibrosis: an indication-restricted FAERS study

Short title: Renal and neuropathy reporting with momelotinib

Article type: Original Research

Authors: Jia Luo^{1*}, Hongxuan Cao²

¹Department of Pharmacy, The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangdong Clinical Research Academy of Chinese Medicine, Guangzhou, Guangdong, China.

²Guangzhou University of Chinese Medicine, The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, Guangdong, China.

*Corresponding author: Jia Luo. E-mail: lawga666@163.com.

Summary word count: 243

Main-text word count: 3378

References: 25

Main figures/tables: 3/2

Supporting figures/tables: 3/12

Summary

Background: Renal dysfunction and peripheral neuropathy have been reported during momelotinib treatment. We examined both outcomes in myelofibrosis (MF) reports using contemporaneous active comparators.

Methods: FDA Adverse Event Reporting System (FAERS) reports initially received from 1 October 2023 to 30 June 2026 were restricted to a primary-suspect study drug with a drug-linked MF indication. Momelotinib was compared with pooled and individual ruxolitinib, fedratinib and pacritinib reports. Co-primary endpoints were the MedDRA 29.0 narrow Standardised MedDRA Queries Acute renal failure and Peripheral neuropathy. We calculated reporting odds ratios (RORs), 95% confidence intervals (CIs), Holm-adjusted primary tests and reporting-characteristic-adjusted estimates.

Results: Among 4,732 reports, 872 involved momelotinib. Renal events were reported in 67 momelotinib and 60 pooled-comparator reports (ROR 5.27, 95% CI 3.69–7.53); peripheral-neuropathy events were reported in 43 and 42 reports (ROR 4.72, 95% CI 3.06–7.26). Both primary Holm-adjusted P values were below 0.001. Adjusted RORs were 2.73 (95% CI 1.81–4.14) and 5.21 (95% CI 3.05–8.90), respectively. Both endpoints remained disproportionately reported after healthcare-professional and US restrictions. The 95% CIs for both fedratinib comparisons included 1. The broad-neuropathy ROR was 2.06 (95% CI 1.49–2.86). Only 19 momelotinib renal reports and one neuropathy report had evaluable event-date intervals.

Conclusion: Momelotinib showed disproportionate reporting for both endpoints, with renal attenuation after adjustment. These findings support focused clinical follow-up but do not establish causality or comparative treatment risk.

Keywords: momelotinib; myelofibrosis; FAERS; pharmacovigilance; renal adverse events; peripheral neuropathy

1 Introduction

The treatment of myelofibrosis (MF) requires attention to anemia as well as splenomegaly and constitutional symptoms. Mometotinib inhibits JAK1/JAK2 and ACVR1/ALK2; its effects on hepcidin provide a rationale for its anemia-related activity.(1) The SIMPLIFY and MOMENTUM trials established its clinical role in JAK-inhibitor-naïve and previously treated populations.(2–4) In the United States, momelotinib is indicated for adults with intermediate- or high-risk primary or secondary MF and anemia.(5) As its use expands, postapproval observations can help identify safety questions that require closer examination in routine care. Renal dysfunction and peripheral neuropathy are two such questions. Neuropathy was described during early clinical development and in the integrated phase III safety analysis.(6,7) More recently, a series of 60 JAK-inhibitor-naïve patients reported a greater than 20% decline in estimated glomerular filtration rate (eGFR) in 17 patients and sensory peripheral neuropathy in 12. The two findings were not associated in that cohort.(8) Other real-world studies have reported creatinine increases, renal insufficiency and neurological adverse events, although their populations, definitions and follow-up differed.(9–11) These observations support evaluating the renal and neurological outcomes separately rather than treating them as a single clinical syndrome.

The FDA Adverse Event Reporting System (FAERS) offers a complementary view of events reported after drug approval. Its value lies in identifying reporting patterns that merit clinical investigation; it does not provide the exposed-patient denominators needed to estimate incidence.(12) For MF, comparisons with the entire FAERS database may also reflect the underlying malignancy and its treatment pathways. An indication-restricted comparison with other drugs used for MF is more closely aligned with the clinical question, although treatment selection and reporting differences remain important.(13) We therefore examined renal-event and peripheral-neuropathy reporting with momelotinib relative to contemporaneous

ruxolitinib, fedratinib and pacritinib reports. Standardized event queries, drug-linked indications and reporting-characteristic analyses were used to assess the consistency and clinical specificity of the findings.

2 Materials and methods

2.1 Data source and study design

We conducted a retrospective case–non-case study using public FAERS quarterly data through the second quarter of 2026. The harmonized source database covered 90 quarters from 2004Q1 to 2026Q2 and contained the demographic, drug, indication, reaction, therapy, outcome and report-source tables. The 2026Q2 release was posted by the FDA on 29 July 2026; the source build was completed on 3 August 2026. FAERS is retained as the name of the historical data source, although the FDA now presents its adverse-event platform as AEMS.(12)

Cumulative FDA deletion lists were applied before retaining the latest valid version of each case. Ties were resolved deterministically, and child-table records were linked to the retained report identifier and source-quarter snapshot. Repeated drug and reaction entries were collapsed for the relevant analysis. The unit of analysis was one retained case report. The study extraction checked file hashes, key uniqueness, linkage and deleted-case identifiers; full processing rules are provided in Supplementary Methods S1. Reporting followed READUS-PV guidance.(14,15)

The analysis specification was recorded before formal comparisons, following an initial feasibility assessment of drug and reaction counts. It was not prospectively registered. Implementation corrections and exploratory additions were documented in the accompanying analysis log.

2.2 Drug identification and study population

Eligible reports had an initial FDA receipt date between 1 October 2023 and 30 June 2026, beginning with the first complete quarter after US momelotinib approval. Eligibility was based on initial receipt rather than the date of a subsequent update. Generic names, active ingredients, brand names and development codes identified the four study drugs (Supplementary Table S1). Explicit topical ruxolitinib products were excluded. For oral brands with contradictory route fields, product identity determined eligibility and the route inconsistency was flagged for sensitivity analysis. Missing route alone did not exclude a report.

The study drug had to be designated primary suspect (PS), with MYELOFIBROSIS or PRIMARY MYELOFIBROSIS recorded as the indication for that same drug sequence. An MF indication attached to another medication did not satisfy this criterion. Reports required at least one reaction record. Known ages below 18 years were excluded; unknown age was retained. Ages outside 0–120 years were treated as missing after conversion of interpretable age units.

Momelotinib reports constituted the exposure group. Eligible ruxolitinib, fedratinib and pacritinib reports formed the pooled active-comparator group and were also examined separately. Reports with more than one eligible PS study drug were excluded to maintain mutually exclusive groups. This design aligned the recorded indication and receipt period, but could not align treatment line, MF severity or baseline organ function.

2.3 Event definitions and report characteristics

The co-primary endpoints were the unmodified, active narrow-scope Standardised MedDRA Queries (SMQs) Acute renal failure and Peripheral neuropathy in English-language MedDRA version 29.0. The queries contained 22 and 45 Preferred Terms (PTs), respectively. Exact PT matches and unambiguous exact lower-level-term mappings were accepted; fuzzy matching

and semantic expansion were not used. Each report was counted once per endpoint, irrespective of the number of matching PTs, and could meet both endpoint definitions. The renal SMQ is an acute-focused retrieval definition rather than a laboratory-adjudicated diagnosis of acute kidney injury (AKI).(16)

Descriptive variables included age, sex, reporter occupation, reporter country, receipt quarter and seriousness/outcome codes. Physicians, pharmacists and other healthcare professionals comprised the healthcare-professional (HCP) group; unknown occupation remained a separate category. Percentages used the full drug-specific report denominator unless otherwise stated. Age summaries used valid recorded ages. Seriousness, hospitalization and death referred to the report as a whole and were not attributed to an individual PT. Baseline characteristics were summarized without significance testing.

2.4 Disproportionality analysis

For each endpoint, cases were reports containing a qualifying PT and non-cases were the remaining eligible reports. We calculated reporting odds ratios (RORs) with log-Wald 95% confidence intervals (CIs). Two-sided Fisher exact tests used the original contingency-table counts. Holm adjustment was applied to the two co-primary tests and, separately, to the six individual-comparator tests.(17) A 0.5 correction to all four cells was specified for estimates and intervals when a table contained a zero cell. Terms unobserved in both groups were assigned $P = 1$ without a substantive ROR estimate. Formulae and multiplicity families are detailed in Supplementary Methods S5.

Exploratory component-PT analyses retained all 67 narrow-query members, including unobserved terms, in one Benjamini–Hochberg family.(18) The main PT display was selected by frequency: at least three momelotinib reports or five pooled-comparator reports, with up to eight frequency-ranked terms per endpoint. Selection did not depend on statistical

significance. RORs describe disproportionate reporting within this selected dataset and should not be interpreted as relative risks.(13)

2.5 Adjustment for reporting characteristics

Secondary logistic models included the study-drug indicator, initial-receipt quarter as a linear index, reporter country (US/non-US) and reporter group (HCP/non-HCP/unknown).

Exponentiated drug coefficients were reported as adjusted RORs with Wald CIs. We checked design-matrix rank, convergence, finite coefficients, extreme estimates and fitting warnings.

Age and sex were not included because their missingness was substantial and differed markedly between drugs. These models assessed recorded reporting characteristics rather than independent clinical risk factors.

2.6 Sensitivity and exploratory specificity analyses

Sensitivity analyses expanded eligibility to PS or secondary-suspect roles, restricted both comparison groups to HCP or US reports, excluded reports co-listing another systemic study JAK inhibitor, removed the MF indication restriction, used source quarter instead of initial receipt, retained all ages, and excluded route-inconsistent reports. Mutual exclusion was reapplied after role expansion; consequently, that analysis was not necessarily a superset of the primary cohort.

The exact PTs Acute kidney injury and Neuropathy peripheral were examined as focused outcome definitions. Exploratory analyses used the complete broad SMQs and a custom four-PT renal-laboratory set (Supplementary Methods S4). A spontaneous-only restriction was unavailable because expedited, periodic and direct submission codes do not establish whether reports were solicited.(19) All sensitivity estimates and analysis-specific denominators are reported.

2.7 Reported event timing and clinical outcomes

Treatment-start-to-event intervals required exactly one distinct, complete valid start date linked to the eligible study drug and a complete report-level event date. Identical repeated starts were collapsed; competing starts and negative intervals were excluded. Partial dates were not imputed. Available intervals were summarized using the median and interquartile range (IQR), with the proportion of reports contributing dates shown explicitly. Because an event date is report-level and event-free follow-up is unavailable, no survival or hazard model was fitted. Co-reported seriousness outcomes and overlap between the two endpoints were summarized descriptively.

2.8 Statistical analysis and software

The primary inferential threshold was a Holm-adjusted P value below 0.05. Component-PT analyses used a false-discovery-rate threshold of 0.05; displayed CIs remained nominal. Sensitivity results were interpreted through their estimates, precision and changed report denominators. Extraction used Python 3.12 and DuckDB 1.5.5; statistical estimation used R 4.6.1. Figures were generated with ggplot2 and assembled with compact, content-dependent spacing. Independent arithmetic checks, model diagnostics and session information are included in the supplementary files.

3 Results

3.1 Study cohort and reporting characteristics

The source database contained 20,588,504 retained reports. The unrestricted momelotinib extraction identified 1,519 reports in any role, including 1,373 with a PS designation. The final study cohort comprised 4,732 reports: 872 for momelotinib, 2,748 for ruxolitinib, 129 for fedratinib and 983 for pacritinib (Figure 1). The three comparator groups contributed 3,860 reports in total.

Reporting characteristics differed considerably by drug (Table 1). HCPs submitted 81.8% of momelotinib reports, compared with 29.2% for ruxolitinib, 51.9% for fedratinib and 15.8% for pacritinib. The proportion from the US ranged from 46.7% for momelotinib to 98.5% for pacritinib. Age was available in 234 momelotinib reports, with a median of 75 years (IQR 69–80). Sex was unknown in 96.8% of ruxolitinib reports. Receipt-quarter counts and reporting composition are provided in Supplementary Table S11 and Supplementary Figure S3.

3.2 Primary renal and peripheral-neuropathy reporting signals

Renal events occurred in 67 of 872 momelotinib reports (7.7%) and 60 of 3,860 comparator reports (1.6%). The crude ROR was 5.27 (95% CI 3.69–7.53). Peripheral-neuropathy events occurred in 43 momelotinib reports (4.9%) and 42 comparator reports (1.1%), yielding an ROR of 4.72 (95% CI 3.06–7.26). Both comparisons met the co-primary Holm-adjusted threshold ($P < 0.001$ for each; Table 2). These percentages refer to submitted reports, not treated-patient event rates.

After adjustment for receipt quarter, country and reporter group, the renal ROR was 2.73 (95% CI 1.81–4.14), whereas the peripheral-neuropathy ROR was 5.21 (95% CI 3.05–8.90) (Figure 2). Both models used all 4,732 reports and converged without recorded fitting warnings. Complete coefficients and diagnostics are presented in Supplementary Tables S6 and S7.

3.3 Individual active-comparator analyses

For renal events, the ROR was 5.50 (95% CI 3.70–8.17) against ruxolitinib, 1.11 (95% CI 0.54–2.28) against fedratinib and 8.10 (95% CI 4.14–15.84) against pacritinib. The corresponding peripheral-neuropathy estimates were 5.23 (95% CI 3.21–8.51), 1.62 (95% CI 0.57–4.59) and 4.58 (95% CI 2.35–8.95) (Figure 2; Supplementary Table S4). Both fedratinib intervals included unity. These smaller-group comparisons were imprecise and did not establish equivalence.

3.4 Component PTs and outcome specificity

Renal impairment was the most frequently reported renal component with momelotinib (31 reports), followed by Acute kidney injury (21) and Renal failure (14). The corresponding pooled-comparator counts were 15, 23 and 20. Neuropathy peripheral accounted for 34 momelotinib and 29 comparator reports. The frequency-selected display contains five PTs; complete results for all 67 narrow-query members are available in Supplementary Tables S2 and S3 (Figure 3).

The exact PT Acute kidney injury yielded an ROR of 4.12 (95% CI 2.27–7.47), and Neuropathy peripheral yielded an ROR of 5.36 (95% CI 3.25–8.85). Broad-query estimates were 4.42 (95% CI 3.23–6.07) for renal events and 2.06 (95% CI 1.49–2.86) for peripheral-neuropathy events. Broadening the neuropathy definition therefore produced a substantially smaller estimate than the narrow query. The custom renal-laboratory set contained 11 momelotinib and 14 comparator reports (ROR 3.51, 95% CI 1.59–7.76; Supplementary Table S5).

3.5 Sensitivity analyses

HCP-restricted analyses yielded RORs of 2.45 (95% CI 1.62–3.69) for renal events and 4.92 (95% CI 2.41–10.05) for peripheral neuropathy. US-only estimates were 4.35 (95% CI 2.33–8.11) and 7.29 (95% CI 4.27–12.44), respectively. After exclusion of reports co-listing another systemic study JAK inhibitor, the corresponding estimates were 5.02 (95% CI 3.44–7.34) and 5.07 (95% CI 3.24–7.93). Full role-expanded, indication-unrestricted, source-quarter and data-quality results are shown in Supplementary Table S5 and Supplementary Figure S1. The renal estimate was particularly sensitive to reporter restriction, consistent with its attenuation in the adjusted model.

3.6 Co-reported outcomes and event timing

One momelotinib report contained both endpoints; 66 contained only the renal endpoint and 42 only peripheral neuropathy. Among the 67 renal-event reports, 66 had a serious outcome code, 24 recorded hospitalization and five recorded death. Among the 43 peripheral-neuropathy reports, 40 had a serious outcome code; none recorded hospitalization or death (Supplementary Tables S9 and S10). These are co-reported outcomes and cannot be assigned specifically to the renal or neurological event.

Usable treatment-start-to-event intervals were available for 19 renal-event reports (28.4%) and one peripheral-neuropathy report (2.3%). The renal median was 18 days (IQR 4–41), including three zero-day intervals. The sole neuropathy interval was also zero days. The renal observations are displayed individually with date completeness in Supplementary Figure S2; no neuropathy timing distribution was estimated (Supplementary Table S8).

4 Discussion

In this indication-restricted FAERS study, renal and peripheral-neuropathy events were reported disproportionately with momelotinib compared with pooled reports involving three other MF JAK inhibitors. The two endpoints differed in their response to adjustment: the renal ROR decreased from 5.27 to 2.73, while the neuropathy estimate remained elevated. HCP restriction produced a similar contrast. This pattern places the reporting population at the center of interpretation and supports discussing the two safety concerns separately.

The renal findings extend a clinically relevant question raised by recent treatment cohorts. The Mayo series documented an eGFR decline from a measured baseline, whereas MoReLife described predominantly low-grade creatinine increases.^(8,9) A cooperative study of 221 patients treated after ruxolitinib failure reported six severe renal toxicities.⁽¹¹⁾ Our narrow SMQ captured an acute-focused reporting phenotype dominated by Renal impairment, Acute kidney injury and Renal failure. The exact AKI and renal-laboratory analyses provided

242 additional context, but neither reconstructs the laboratory trajectories used in clinical studies.

243 FAERS cannot determine whether an individual report reflected pre-existing dysfunction, an

244 acute intercurrent illness or a treatment-emergent change.

245 Background renal morbidity is particularly relevant in MF. A separate cohort found chronic

246 kidney disease in 26.1% of patients and associated reduced renal function with adverse

247 outcomes.(20) Infection, altered hemodynamics, concomitant treatments and disease

248 progression may therefore contribute to renal reports independently of momelotinib. A single-

249 dose pharmacokinetic study did not identify an exposure change in renal impairment requiring

250 routine dose adjustment, but this does not resolve the effects of prolonged treatment or

251 changing renal function.(21) The present signal supports clinically adjudicated follow-up; it

252 does not provide a basis for changing renal dosing recommendations.

253 The neuropathy finding is more closely aligned with an established part of momelotinib's

254 safety profile. The integrated phase III analysis reported peripheral neuropathy in 107 of 725

255 exposed patients, including nine grade 3 or higher events, without an increasing incidence

256 across successive observation periods.(7) An earlier 100-patient series reported neuropathy in

257 44 patients, with a median onset of 32 weeks.(6) Differences in exposure duration and

258 ascertainment are important when comparing those clinical observations. Their percentages

259 cannot be directly compared with FAERS reporting proportions. An electrophysiologically

260 characterized sensory axonal neuropathy case provides further clinical description, although a

261 single case cannot establish a general treatment-switching strategy.(22)

262 The narrower neuropathy query produced a stronger reporting association than the broad

263 query. Broader retrieval includes less-specific manifestations that may be common across MF

264 treatment populations, so dilution of the association is plausible. Differential coding and

265 ascertainment could produce the same pattern. Retaining both analyses clarifies how the result

266 depends on the outcome definition without treating a standardized query as a confirmed
267 neurological diagnosis.

268 Exposure–response analyses offer a possible connection worth examining in future clinical
269 work: greater total-active-moiety exposure was associated with higher neuropathy odds, and
270 baseline creatinine clearance was a covariate of active-metabolite clearance.(23) Our data
271 cannot test whether renal dysfunction mediates neurological toxicity. Only one momelotinib
272 report contained both endpoints, and sparse co-reporting cannot exclude shared susceptibility.
273 Establishing such a relationship would require repeated renal measurements, treatment
274 exposure, neurological examination and reliable temporal ordering.

275 Comparator choice also affected the interpretation. Ruxolitinib contributed most of the pooled
276 comparator reports, while fedratinib contributed only 129. Neither endpoint showed a precise
277 reporting difference against fedratinib. Pacritinib reports, in turn, were predominantly from
278 US and non-HCP sources. These distributions demonstrate why the pooled result cannot be
279 generalized to a uniform difference from every MF JAK inhibitor. Aligning indication and
280 calendar period improves the relevance of the comparison but does not align anemia, platelet
281 count, prior treatment, prescribing volume or monitoring intensity.(13) The lower adjusted
282 renal estimate is consistent with sensitivity to measured reporting characteristics; it cannot be
283 converted into the proportion of an association explained by confounding, because marginal
284 and conditional odds ratios are not directly collapsible.(24)

285 Acute kidney injury and peripheral neuropathy already appear in momelotinib regulatory
286 safety information.(5) The contribution of this study is therefore a focused comparison of
287 postapproval reporting, with explicit indication linkage, complete component-term results and
288 examination of reporting-source differences. The clinical next step is a longitudinal
289 comparison in similar MF treatment settings, documenting baseline renal reserve, serial renal
290 measures, intercurrent illness and structured neurological assessment. Reasons for selecting

291 each JAK inhibitor and subsequent treatment changes would be essential to distinguish
292 treatment effects from channeling.

293 Event-date completeness limits what this study can contribute about timing. The median renal
294 interval of 18 days came from 19 reports, and only one neuropathy report had evaluable dates.
295 A report-level event date may refer to another reaction or to a pre-existing problem; same-day
296 entries are particularly difficult to interpret. These data cannot establish an early high-risk
297 window or contradict the later neuropathy observed in clinical cohorts. Displaying the
298 individual renal intervals alongside the missing-date burden is more informative here than
299 fitting an onset model.

300 Several limitations remain. FAERS is affected by underreporting, selective and stimulated
301 reporting, incomplete clinical information and possible duplicate submissions under different
302 case identifiers. Publicity and known labeling can influence which events are reported.(25)
303 Solicited and spontaneous reporting origins could not be reliably separated.(19) Demographic
304 missingness differed sharply by drug, and the adjusted models lacked baseline renal function,
305 hemoglobin, platelet count, MF risk category and treatment history. Retaining unknown age
306 avoided extensive exclusion but means that not all reports were confirmed to concern adults.
307 Requiring an explicit drug-linked MF indication may additionally select better-documented
308 reports.

309 The endpoints were not clinically adjudicated, and correlated PTs may describe the same
310 episode. Seriousness codes belong to the whole report; an absent code does not establish that
311 a clinical outcome did not occur. Narrow queries may miss relevant presentations, while
312 broader definitions reduce specificity. The analysis followed feasibility inspection rather than
313 prospective registration, and the overlapping sensitivity analyses are not independent
314 replications. Finally, confidence intervals quantify sampling variation within the selected
315 reports, not uncertainty from reporting bias. Confirmation in an independent, exposure-

defined clinical dataset is required before estimating absolute risk or recommending differential monitoring schedules.

5 Conclusion

Renal events and peripheral neuropathy showed disproportionate reporting with momelotinib in contemporaneous, indication-linked MF reports. Renal estimates attenuated after reporting-characteristic adjustment, and the pooled findings did not translate into a clear difference against every individual comparator. These results support separate clinical evaluation of the two safety concerns, while remaining insufficient to establish causality or quantify comparative treatment risk.

Statements and declarations

Author Contributions

Jia Luo: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. Hongxuan Cao: Validation, Writing – review & editing.

Ethics and consent

This secondary analysis used publicly available, de-identified adverse-event reports and involved no participant recruitment, intervention or collection of identifiable information. Individual consent was not obtained for this secondary analysis.

Conflicts of interest

None.

Funding

None.

Data availability statement

Public quarterly data are available from the FDA. Aggregate results, study extraction and analysis scripts, revised plotting code and source-build metadata are provided in Supplementary Code 1. The scripts require the documented harmonized Parquet schema and

341 are not a standalone reconstruction of the upstream raw-file cleaning process. Report-level
342 working caches and the licensed full MedDRA distribution are not redistributed.

343 **Artificial-intelligence disclosure**

344 During the preparation of this work, the authors used OpenAI Codex solely for language
345 refinement and assistance with the development and debugging of R visualization code. All
346 AI-assisted text and code were reviewed and verified by the authors, who take full
347 responsibility for the content of the article. All figures were generated programmatically from
348 the study data using R, ggplot2, and patchwork; no generative AI image-generation tools were
349 used.

350 **Acknowledgements**

351 None.

352 **Clinical trial number**

353 Not applicable.

354

355 References

- 356 1. Asshoff, M., Petzer, V., Warr, M. R., Haschka, D., Tymoszek, P., Demetz, E. Momelotinib
357 inhibits ACVR1/ALK2, decreases hepcidin production, and ameliorates anemia of chronic
358 disease in rodents. *Blood*. 2017;129(13):1823–30. doi:10.1182/blood-2016-09-740092
359 PubMed PMID: 28188131; PubMed Central PMCID: PMC5693322.
- 360 2. Mesa, R. A., Kiladjian, J. J., Catalano, J. V., Devos, T., Egyed, M., Hellmann, A.
361 SIMPLIFY-1: A Phase III Randomized Trial of Momelotinib Versus Ruxolitinib in Janus
362 Kinase Inhibitor-Naive Patients With Myelofibrosis. *J Clin Oncol*. 2017;35(34):3844–50.
363 doi:10.1200/JCO.2017.73.4418 PubMed PMID: 28930494; PubMed Central PMCID:
364 PMC6553796.
- 365 3. Harrison, C. N., Vannucchi, A. M., Platzbecker, U., Cervantes, F., Gupta, V., Lavie, D.
366 Momelotinib versus best available therapy in patients with myelofibrosis previously treated
367 with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial. *Lancet Haematol*.
368 2018;5(2):e73–81. doi:10.1016/S2352-3026(17)30237-5 PubMed PMID: 29275119.
- 369 4. Verstovsek, S., Gerds, A. T., Vannucchi, A. M., Al-Ali, H. K., Lavie, D., Kuykendall, A.
370 T. Momelotinib versus danazol in symptomatic patients with anaemia and myelofibrosis
371 (MOMENTUM): results from an international, double-blind, randomised, controlled, phase
372 3 study. *Lancet*. 2023;401(10373):269–80. doi:10.1016/S0140-6736(22)02036-0 PubMed
373 PMID: 36709073.
- 374 5. GlaxoSmithKline LLC. OJJAARA (momelotinib) tablets: US prescribing information
375 [Internet]. GlaxoSmithKline LLC; 2026. Available from:
376 [https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=4a672fd1-eb7b-4aa9-](https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=4a672fd1-eb7b-4aa9-9b23-845e4b5dc400)
377 [9b23-845e4b5dc400](https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=4a672fd1-eb7b-4aa9-9b23-845e4b5dc400)
- 378 6. Abdelrahman, R. A., Begna, K. H., Al-Kali, A., Hogan, W. J., Litzow, M. R., Pardani, A.
379 Momelotinib treatment-emergent neuropathy: prevalence, risk factors and outcome in
380 100 patients with myelofibrosis. *Br J Haematol*. 2015;69(1):77–80. doi:10.1111/bjh.13262
381 PubMed PMID: 25511866.
- 382 7. Verstovsek S, Mesa R, Gupta V, Lavie D, Dubruille V, Cambier N, et al. Momelotinib
383 long-term safety and survival in myelofibrosis: integrated analysis of phase 3 randomized
384 controlled trials. *Blood Advances*. 2023 Jul 25;7(14):3582–91.
385 doi:10.1182/bloodadvances.2022009311
- 386 8. Tefferi, A., Abdelmagid, M., Palmer, J. M., Al-Kali, A., Yi, C. Y. A., Matin, A. Post-FDA
387 Approval Experience With Momelotinib in JAK Inhibitor-Naive Myelofibrosis: Focus on
388 Anemia Response and Treatment-Emergent Nephropathy and Peripheral Neuropathy. *Am J*
389 *Hematol*. 2026;101(3):570–6. doi:10.1002/ajh.70203 PubMed PMID: 41504170.
- 390 9. Jilg, S., Schwaab, J., Sockel, K., Crodel, C. C., Brueckl, V., Stegelmann, F. MoReLife -
391 real-life data support the potential of momelotinib as a safe and effective treatment option
392 for cytopenic myelofibrosis patients. *Ann Hematol*. 2024;103(10):4065–77.
393 doi:10.1007/s00277-024-05908-4 PubMed PMID: 39073589.
- 394 10. Pérez-Lamas L, Segura Diaz A, García Delgado R, Álvarez-Larrán A, Senin MA, Mora E,
395 et al. Real world outcomes of momelotinib in myelofibrosis patients with anemia: results

- from the MOMGEMFIN study. *Blood Cancer J.* 2025 Apr 17;15(1):67.
doi:10.1038/s41408-025-01275-z
11. Palandri F, Marchetti M, Elli EM, Isidori A, Ganesello I, Sartor C, et al. Clinical benefit and predictors of response to momelotinib after ruxolitinib failure: A cooperative real-world study. *Cancer.* 2026 May 15;132(10):e70457. doi:10.1002/cncr.70457
12. US Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) Database and AEMS Public Dashboard FAQs [Internet]. US Food and Drug Administration; 2026. Available from: <https://www.fda.gov/drugs/drug-approvals-and-databases/fda-adverse-event-reporting-system-faers-database>
13. Faillie, J. L. Case-non-case studies: Principle, methods, bias and interpretation. *Therapie.* 2019;74(2):225–32. doi:10.1016/j.therap.2019.01.006 PubMed PMID: 30773344.
14. Fusaroli M, Salvo F, Begaud B, AlShammari TM, Bate A, Battini V, et al. The Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in Pharmacovigilance (READUS-PV): Development and Statement. *Drug Saf.* 2024 Jun;47(6):575–84. doi:10.1007/s40264-024-01421-9
15. Fusaroli M, Salvo F, Begaud B, AlShammari TM, Bate A, Battini V, et al. The REporting of A Disproportionality Analysis for DrUg Safety Signal Detection Using Individual Case Safety Reports in Pharmacovigilance (READUS-PV): Explanation and Elaboration. *Drug Saf.* 2024 Jun;47(6):585–99. doi:10.1007/s40264-024-01423-7
16. International Council for Harmonisation. Introductory Guide for Standardised MedDRA Queries (SMQs), Version 29.0 [Internet]. International Council for Harmonisation (ICH); 2026. Available from: https://alt.meddra.org/files_acrobat/SMQ_intguide_29_0_English.pdf
17. Holm, S. A Simple Sequentially Rejective Multiple Test Procedure. *Scand J Stat.* 1979;6(2):65–70.
18. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc Series B Stat Methodol.* 1995;57:289–300. doi:10.1111/j.2517-6161.1995.tb02031.x
19. Jokinen JD, Walley RJ, Colopy MW, Hilzinger TS, Verdru P. Pooling Different Safety Data Sources: Impact of Combining Solicited and Spontaneous Reports on Signal Detection In Pharmacovigilance. *Drug Saf.* 2019 Oct;42(10):1191–8. doi:10.1007/s40264-019-00843-0
20. Lucijanic, M., Galusic, D., Krecak, I., Sedinic, M., Holik, H., Perisa, V. Reduced renal function strongly affects survival and thrombosis in patients with myelofibrosis. *Ann Hematol.* 2020;99(12):2779–85. doi:10.1007/s00277-020-04239-4 PubMed PMID: 32862283.
21. Xin, Y., Kawashima, J., Weng, W., Kwan, E., Tarnowski, T., Silverman, J. A. Pharmacokinetics and Safety of Momelotinib in Subjects With Hepatic or Renal Impairment. *J Clin Pharmacol.* 2018;58(4):522–32. doi:10.1002/jcph.1050 PubMed PMID: 29283448.

- 436 22.Torregrosa Diaz JM, Cailly L, Gallego Hernanz MP, Gardeney H, Cayssials E.
437 Rechallenge of ruxolitinib after momelotinib-related toxicity in a 74-yo woman with
438 secondary myelofibrosis: a case report. *Front Med.* 2026 Jul 1;13:1878696.
439 doi:10.3389/fmed.2026.1878696
- 440 23.Rich B, Srinivasan M, Ho YL, Visser SAG, Ferron-Brady G, Vlasakakis G. Population
441 Pharmacokinetics and Exposure–Response Analyses of Momelotinib, Its Active Metabolite
442 (M21), and Total Active Moiety in Myelofibrosis. *Clin Pharma and Therapeutics.* 2026
443 Mar;119(3):629–40. doi:10.1002/cpt.70076
- 444 24.Greenland, S., Robins, J. M., Pearl, J. Confounding and Collapsibility in Causal Inference.
445 *Stat Sci.* 1999;14(1):29–46. doi:10.1214/ss/1009211805
- 446 25.de Boissieu, P., Kanagaratnam, L., Abou Taam, M., Drame, M., Trenque, T., Roux, M. P.
447 Notoriety bias in a database of spontaneous reports: the example of osteonecrosis of the
448 jaw under bisphosphonate therapy in the French national pharmacovigilance database.
449 *Pharmacoepidemiol Drug Saf.* 2014;23(9):989–92. doi:10.1002/pds.3622 PubMed PMID:
450 24737486.

451

Table 1. Baseline characteristics of eligible myelofibrosis reports

Characteristic	Momelotinib N = 872	Ruxolitinib N = 2,748	Fedratinib N = 129	Pacritinib N = 983
Reports, n	872	2,748	129	983
Age				
Age available	234 (26.8)	828 (30.1)	119 (92.2)	623 (63.4)
Age, median (IQR), years	75 (69–80)	73.5 (65–80)	74 (68–79)	73 (65–79)
Sex				
Female	223 (25.6)	46 (1.7)	52 (40.3)	312 (31.7)
Male	261 (29.9)	42 (1.5)	68 (52.7)	351 (35.7)
Sex unknown	388 (44.5)	2,660 (96.8)	9 (7.0)	320 (32.6)
Reporter type				
Healthcare professional	713 (81.8)	802 (29.2)	67 (51.9)	155 (15.8)
Non-healthcare professional	57 (6.5)	879 (32.0)	42 (32.6)	764 (77.7)
Reporter unknown	102 (11.7)	1,067 (38.8)	20 (15.5)	64 (6.5)
Reporter country				
US reporter country	407 (46.7)	1,961 (71.4)	75 (58.1)	968 (98.5)
Non-US reporter country	465 (53.3)	787 (28.6)	54 (41.9)	15 (1.5)
Co-reported outcomes				
Serious outcome reported	678 (77.8)	1,653 (60.2)	92 (71.3)	394 (40.1)
Death reported	162 (18.6)	385 (14.0)	14 (10.9)	127 (12.9)
Hospitalization reported	219 (25.1)	558 (20.3)	32 (24.8)	208 (21.2)

Values are n (%) unless otherwise indicated. Percentages use the full drug-specific report denominator; age summaries use only valid recorded ages. Unknown age was retained after exclusion of known age below 18 years. Seriousness, death and hospitalization refer to the entire report and may overlap. IQR, interquartile range.

Table 2. Co-primary endpoint counts and crude and adjusted reporting odds ratios

Endpoint (narrow SMQ)	Momelotinib event / non-event	Pooled comparator event / non-event	Crude ROR (95% CI)	Adjusted ROR (95% CI)
Acute renal failure	67 / 805	60 / 3,800	5.27 (3.69–7.53)	2.73 (1.81–4.14)
Peripheral neuropathy	43 / 829	42 / 3,818	4.72 (3.06–7.26)	5.21 (3.05–8.90)

Comparator: pooled disjoint ruxolitinib, fedratinib and pacritinib reports. Holm-adjusted two-sided Fisher P values for the two primary tests: renal 1.89e-18; neuropathy 1.25e-11. Crude CIs use the log-Wald method without continuity correction (no zero cells). Adjusted models include receipt quarter (linear), US/non-US reporter country and reporter group; adjusted CIs are nominal Wald CIs. The SMQs are retrieval definitions, not adjudicated diagnoses. ROR, reporting odds ratio; CI, confidence interval; SMQ, Standardised MedDRA Query.

Figure 1. Selection of the myelofibrosis reporting cohort

Counts before final allocation represent drug-report memberships and may overlap across drugs. Reports were selected by initial FDA receipt from 1 October 2023 to 30 June 2026, primary-suspect drug status, systemic formulation and a myelofibrosis indication linked to the same drug sequence. Two reports with a known age below 18 years were excluded; age-unknown reports were retained. No report met the exclusion for more than one eligible study-drug primary-suspect membership. The final cohort contained 872 momelotinib reports and 3,860 comparator reports. MF, myelofibrosis; PS, primary suspect.

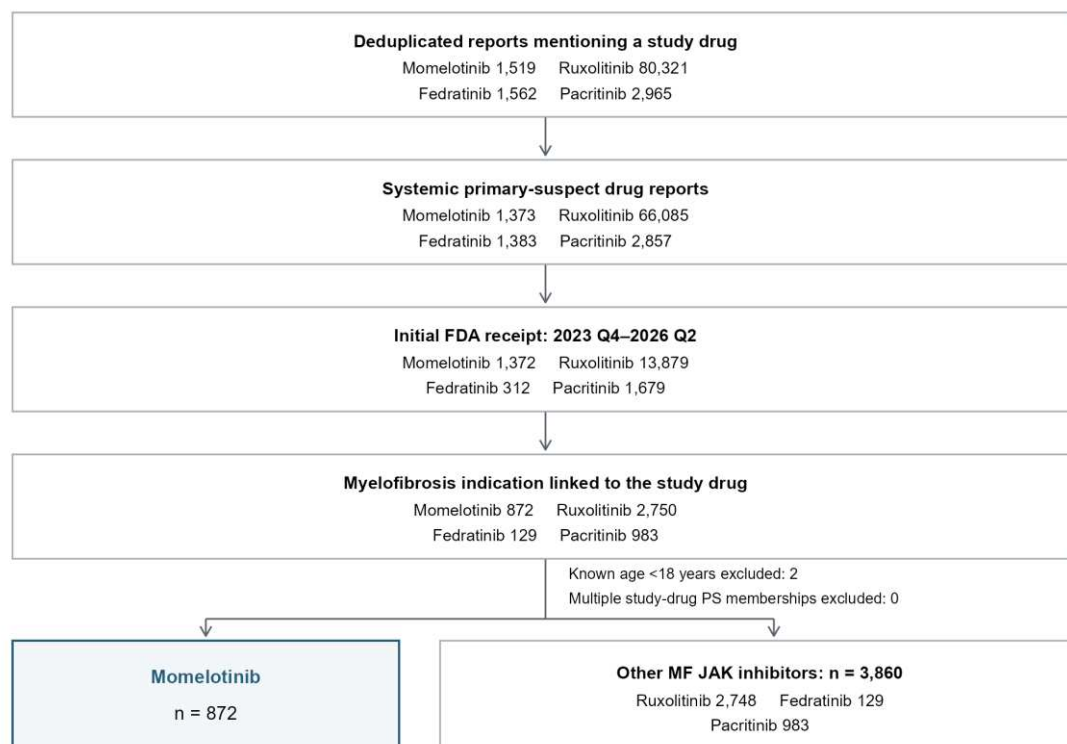


Figure 2. Renal and peripheral-neuropathy reporting odds with momelotinib

(a) Narrow Acute renal failure SMQ. (b) Narrow Peripheral neuropathy SMQ. Circles show crude reporting odds ratios (RORs); diamonds show adjusted RORs. Horizontal lines indicate nominal 95% confidence intervals. Blue and teal identify the renal and neuropathy endpoints; grey identifies secondary individual-comparator estimates. Counts are endpoint-positive reports divided by all eligible reports in each comparison. Adjustment included initial-receipt quarter, US versus non-US reporting country and reporter category. Two-sided Fisher exact P values were Holm-adjusted separately for the two primary endpoint tests and the six secondary individual-comparator tests; this did not alter the displayed intervals. The dashed line denotes ROR = 1. Both panels use the same logarithmic scale. Individual comparisons were not used to establish equivalence between drugs. SMQ, Standardised MedDRA Query.

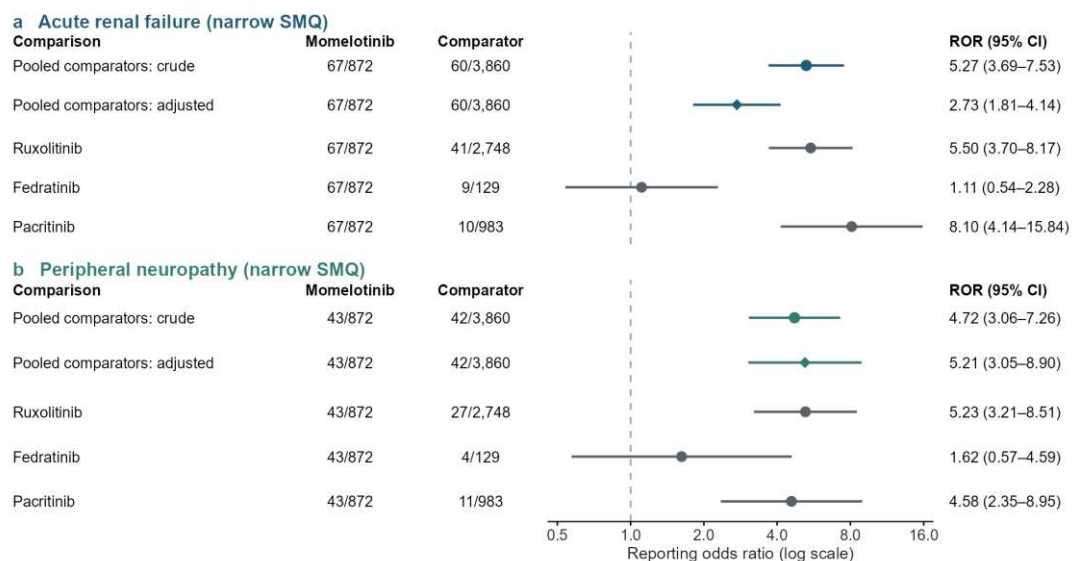
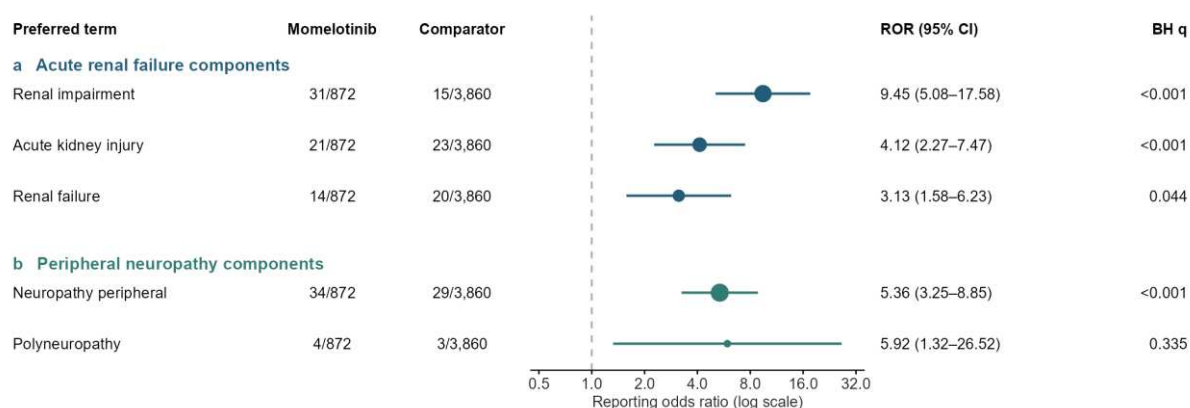


Figure 3. Preferred terms contributing to the two primary endpoints

(a) Renal terms. (b) Peripheral-neuropathy terms. The five terms were selected by frequency, requiring at least three momelotinib reports or five pooled-comparator reports, with up to eight terms per endpoint. Selection did not depend on statistical significance. Circle area is proportional to the number of momelotinib reports containing each term. Counts are term-positive reports divided by all eligible reports (872 momelotinib; 3,860 pooled comparators). Horizontal lines show crude reporting odds ratios (RORs) and 95% confidence intervals on a logarithmic scale; the dashed line denotes ROR = 1. BH q values are Benjamini–Hochberg-adjusted two-sided Fisher exact P values from the complete 67-term testing family, not from the five displayed terms. A report may contain more than one preferred term.



Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Renaleventsandperipheralneuropathyreportedwithmomelotinibinmyelofibrosisindicatsupplementary.docx](#)