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Public Origin-Market Prices and Global Access to Chinese-Origin Oncology Medicines: An Exploratory Multiple-Case Study

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Abstract

Affordable access to cancer medicines depends not only on clinical value but also on the pricing and reimbursement arrangements adopted as products expand across markets. We conducted an exploratory multiple-case study of four Chinese-origin oncology medicines—zanubrutinib, fruquintinib, tislelizumab, and efbemalenograstim alfa—to examine whether a low, publicly visible origin-market price could create international price-reference exposure. We compared reported public unit prices across approved markets, summarised monthly medicine acquisition costs from labelled dosing schedules, and triangulated approval timing with entry into the China National Reimbursement Drug List. China had the lowest observed public price for every medicine at market exchange rates; the observed country sets differed by medicine. Three medicines were first approved in China and expanded later to the United States and/or Europe, and all four entered the NRDL. The Chinese-origin product had a lower reported median monthly acquisition cost in three of four comparator pairs. These findings document a visible origin-market price anchor rather than a demonstrated causal effect on foreign prices, launch timing, or clinical value. For oncology pharmacy and health-system decision makers, price transparency and reimbursement design should support patient access while preserving the conditions for sustainable international availability of innovative cancer medicines.

Keywords: Chinese-origin medicines; oncology; external reference pricing; launch sequencing; cross-national price comparison; national reimbursement drug list; price spillover

1. Introduction

China has become both a major market for innovative medicines and an increasingly important source of globally developed pharmaceutical products. This transition changes the policy question surrounding Chinese pharmaceutical prices. In addition to domestic affordability, it raises the question of how prices observable in China might inform negotiations when Chinese-origin medicines expand internationally [1].

China's basic medical insurance arrangements include employee and resident schemes, while the National Healthcare Security Administration (NHSA) coordinates the national reimbursement drug list (NRDL). For exclusive medicines, access negotiations establish payment standards; expert assessment considers clinical and pharmacoeconomic evidence and fund affordability. National listing does not mean full reimbursement: patient cost sharing and implementation depend on local benefit arrangements and reimbursement restrictions. Negotiated medicines enter procurement and dispensing arrangements that

Check for updates

Academic Editor: Andrea Zovi

Received: 23 September 2026
Revised: 24 October 2026
Accepted: 26 October 2026
Published: 29 October 2026

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link reimbursement to access [2,3]. In the 2020 adjustment, 119 medicines were successfully negotiated, with an average price reduction of 50.64%; this is an aggregate across successful negotiations, not an oncology-specific estimate [4]. Zanubrutinib and tislelizumab entered the 2020 NRDL round, fruquintinib the 2019 round, and efbemalenograstim alfa the 2023 round. The negotiation year, publication date, and implementation date must be distinguished.

External reference pricing (ERP) uses prices of the same medicine in selected foreign jurisdictions to inform domestic price setting or negotiation [5–7]. A payer selects a country basket, identifies a comparable strength and presentation at a specified distribution-chain level, converts currencies and applies a rule such as the minimum, average or median price. Subsequent reviews can transmit later price changes. The result depends on basket membership, price definition, exchange rates and review frequency; formal ERP differs from informal use of foreign prices in negotiation. Confidential rebates can make public prices imperfect proxies for actual payments. For example, in a hypothetical three-country basket with comparable public prices of 100, 60 and 30, a minimum-price rule yields 30 and an arithmetic-mean rule approximately 63.3; neither identifies the confidential net price. This example illustrates the mechanism and is not a finding for the four medicines [5].

Previous research addresses related but distinct questions. Danzon and Towse discuss differential pricing as a way to reconcile access and research incentives [8], while Danzon et al. examine price regulation and launch timing across established pharmaceutical markets [9]. Kanavos et al. show that ERP outcomes depend on implementation [5]. In China, studies of reimbursement negotiation examine changes in medicine use, prices, and spending [10–13], while Lyu et al. compare 140 negotiated innovative medicines across 15 countries using multiple price indices [14], and Pan et al. compare list prices and clinical value in China, Japan, and South Korea [15]. These studies establish the relevance of reimbursement, economic burden [16], and international price differences, but do not establish that a Chinese-origin medicine's domestic price caused a foreign pricing decision. The present analysis adds a product-origin and timing perspective: it links observable price positions to regulatory and reimbursement sequences for four internationally expanding assets, rather than estimating a population-wide price effect.

We use the term home-market price-reference exposure for the possibility that a low, observable origin-market price informs foreign negotiations. The expression home-market price penalty describes a hypothesised adverse outcome of that exposure, not an outcome demonstrated here. We address three questions: (1) how do publicly available Chinese prices compare with prices in other observed approved markets; (2) how do Chinese reimbursement milestones relate to international regulatory expansion; and (3) what hypotheses and contracting considerations arise from this configuration?

The study distinguishes nominal price differences relevant to cross-border comparisons from purchasing-power-parity (PPP) adjustments that contextualise domestic price levels. It also distinguishes regulatory approval, reimbursement listing and observed price availability, which are separate events. Section 2 presents the conceptual framework; Section 3 describes case selection and methods; Section 4 reports descriptive findings; Section 5 discusses interpretation, practical implications and limitations; and Section 6 concludes.

2. Conceptual Framework

2.1. From Differential Pricing to Reverse Price Spillovers

Differential pricing can support access when prices reflect countries' financing capacity [8]. ERP can potentially transmit a concession beyond its intended market, depending on the reference rule and whether the relevant price is observable [5,6]. An indirect transmission route would require evidence that an intermediate market incorporates the Chinese

price and is itself referenced elsewhere. Neither such a route nor direct formal inclusion of China in the relevant country baskets is demonstrated for these cases. Informal negotiating use remains a separate hypothesis.

2.2. Home-Market Price-Reference Exposure

The proposed exposure mechanism requires an observable origin-market price, subsequent foreign pricing opportunities, and a potential route through formal referencing or informal benchmarking. NRDL inclusion alone does not establish public disclosure: the 2020 NRDL notice specifically restricts public dissemination of payment standards marked as confidential [3]. Consequently, a later observable procurement or list price cannot automatically be treated as the payment standard first disclosed on the date of NRDL entry. The cross-sectional price snapshot and reimbursement chronology identify possible overlap, rather than the date or extent of actual price transmission.

Three propositions guide future investigation. Earlier availability of a low origin-market price relative to foreign pricing decisions may increase reference exposure; a publicly disclosed concession may create different exposure from a confidential net rebate; and firms anticipating exposure may adjust launch or contracting decisions. Testing these propositions requires dated price records, payer rules and decision-level evidence. The present study provides descriptive case evidence consistent with possible exposure, without testing these causal or behavioural propositions.

3. Methods

3.1. Study Design and Case Selection

We used an exploratory multiple-case design combining cross-sectional public-price comparisons with regulatory and reimbursement timelines. Medicines were selected through a three-stage screening process. First, an initial pool of 12 Chinese-origin innovative medicines was identified on the basis of development by a China-based company and marketing approval in at least one major overseas country or region before December 2024. Second, candidates were excluded if they were outside oncology and supportive oncology care, had neither NRDL inclusion nor implemented basic medical insurance reimbursement in China before December 2024, or had too few overseas price observations or insufficiently comparable public price information for cross-national analysis. Where several candidates shared the same target or mechanism, representative medicines were retained to limit overrepresentation of a single pharmacological class. This process yielded four cases: zanubrutinib, fruquintinib, tislelizumab and efbemalenograstim alfa. Third, four comparator medicines were selected, prioritising products used in reimbursement negotiation or market-access submissions and, where possible, matching the indication and mechanism of action and having established international use (Section 3.5).

This selection linked Chinese reimbursement experience with observable overseas prices while covering distinct therapeutic classes, small molecules and biologics, and both anticancer treatment and supportive care. It also captured different internationalisation pathways, including US-first and China-first approvals. The sample supports analytical comparison across informative cases rather than population-level estimates or an exhaustive assessment of Chinese-origin medicines. Chinese-origin refers to development origin, not necessarily the country of first approval or first-in-class status. Table 1 summarises the four medicines and their principal clinical uses.

Table 1. Case characteristics and internationalisation sequence.

Medicine	Class	First Approvals	China NRDL Entry	Internationalisation Pathway	Principal Clinical Use
Zanubrutinib (Brukinsa)	BTK inhibitor	US November 2019; China June 2020	2020 round	US-first approval; subsequent China reimbursement and overseas expansion	B-cell malignancies: MCL, WM, MZL, CLL/SLL and FL.
Fruquintinib (Elunate/Fruzaqla)	VEGFR inhibitor	China September 2018; US November 2023	2019 round	China-first approval; extended interval before US approval	Previously treated metastatic colorectal cancer.
Tislelizumab (Tevimbra)	PD-1 antibody	China December 2019; EU September 2023; US March 2024	2020 round	China-first approval; NRDL entry before EU and US approvals	Advanced oesophageal squamous cell carcinoma and gastric or gastro-oesophageal junction adenocarcinoma.
Efbemalenograstim alfa (Ryzneuta)	Long-acting G-CSF	China May 2023; US November 2023; EU March 2024	2023 round	China-first approval; rapid US and EU expansion	Prevention of chemotherapy-associated febrile neutropenia in adults with non-myeloid malignancies.

Sources: regulatory records and first-approval reports [1,17–22]; authors' synthesis. Clinical uses are selected indications, not exhaustive label summaries; approval dates, treatment lines, and combination requirements vary by jurisdiction. FL treatment with zanubrutinib requires an indication-specific combination regimen. NRDL entry refers to the negotiation round, not its implementation date. BTK, Bruton's tyrosine kinase; VEGFR, vascular endothelial growth factor receptor; PD-1, programmed death 1; G-CSF, granulocyte colony-stimulating factor; MCL, mantle cell lymphoma; WM, Waldenstrom macroglobulinaemia; MZL, marginal zone lymphoma; CLL/SLL, chronic lymphocytic leukaemia/small lymphocytic lymphoma; FL, follicular lymphoma.

3.2. Price and Country Data

Countries were included separately for each medicine when marketing authorisation and a publicly verifiable price were available. The source framework comprised official government price databases and government-recognised price sources. These observations are public list, reimbursement, or procurement benchmarks as defined by their sources; they omit undisclosed rebates and are not harmonised ex-manufacturer net transaction prices. The United States was not included in the original cross-sectional dataset because a comparable price series was unavailable within that extraction framework. List-to-net divergence also affects other countries and is not a uniquely US justification for exclusion. US wholesale acquisition cost (WAC), an undiscounted manufacturer benchmark, is therefore considered separately as context and is not pooled with the analytical observations.

The analytical price date was 26 November 2024. Local prices were converted to US dollars using contemporaneous exchange rates, and the smallest marketed pack was standardised to the dose unit used in the source analysis. Monthly medicine acquisition costs were derived from labelled dose and administration frequency. Such estimates exclude administration, monitoring, adverse-event management and other healthcare costs. Reproducibility requires a medicine-country source log with price type, observation date, currency, strength and pack size, together with the exchange-rate and PPP series and explicit dosing and cycle assumptions; these inputs cannot be inferred from regulatory approval dates.

3.3. Nominal Prices and Affordability-Adjusted Prices

Nominal US-dollar prices and PPP-adjusted prices answer different questions. Nominal prices describe visible cross-market price positions relevant to possible international referencing, but not realised manufacturer revenue. PPP adjustment contextualises prices against general domestic price levels; it does not measure household affordability, insurance coverage or patient out-of-pocket expenditure. For country i, the nominal price equals the

local-currency price divided by the exchange rate in local currency per US dollar. The PPP-adjusted price equals the local-currency price divided by the World Bank PPP conversion factor and is expressed in international dollars, not transaction US dollars. Comparisons depend on the year and type of PPP series used.

3.4. Regulatory and Reimbursement Sequence

For each medicine, we recorded the first verified approval in China, the United States, and the European Union, together with the first NRDL inclusion. Dates were triangulated using regulatory agency records, peer-reviewed first-approval reports and manufacturer announcements. The sequence was used to classify cases as China-first or overseas-first and to identify whether the lower reimbursed Chinese price became visible before major-market expansion.

3.5. Comparator Analysis

The descriptive comparators were ibrutinib for zanubrutinib, regorafenib for fruquintinib, pembrolizumab for tislelizumab, and pegfilgrastim for efbemalenograstim alfa. These pairs contextualise medicine acquisition costs; they are not assumed to have identical indications, treatment lines, effectiveness or safety. No new comparative-efficacy or cost-effectiveness analysis was conducted. Such analysis would require an indication-specific population, appropriate clinical comparator, comparative survival or other relevant outcomes, adverse events, utilities, total costs, perspective, time horizon and willingness-to-pay threshold. For example, the ALPINE trial provides head-to-head evidence for zanubrutinib and ibrutinib in relapsed or refractory chronic lymphocytic leukaemia [23], but its findings cannot be transferred to the other pairs or all indications. Acquisition-price differences alone do not establish cost-effectiveness or clinical undervaluation.

3.6. Statistical Analysis

The analysis was descriptive. Country-specific public-price positions and pair-specific median acquisition costs were summarised separately because country coverage differed by medicine. Observations were clustered by medicine and country and did not constitute independent observations from a common treatment class. No pooled rank-test inference was used to claim class-wide clinical or economic differences. Statistical summaries were generated using SPSS version 26.0.

4. Results

4.1. Characteristics and Internationalisation Pathways

The four cases followed two distinct regulatory pathways. Zanubrutinib was first approved in the United States in November 2019 and in China in June 2020. In contrast, fruquintinib, tislelizumab, and efbemalenograstim alfa received their first global approvals in China, followed by entry into the United States and/or European Union. Fruquintinib had the longest China-to-US interval, from September 2018 to November 2023. Tislelizumab was approved in China in December 2019, in the European Union in September 2023, and in the United States in March 2024. Efbemalenograstim alfa was approved in China in May 2023, followed by the United States in November 2023 and the European Union in March 2024.

4.2. Cross-National Price Position

At market exchange rates, China was the lowest observed public-price market for all four medicines (Figure 1). For zanubrutinib, the Chinese unit price was US $11.63, compared with US $93.94 in Austria, US $51.09 in Germany and US $46.83 in Norway. These

observations describe the recorded public-price position, not a common net discount or evidence that one country's price determined another's.

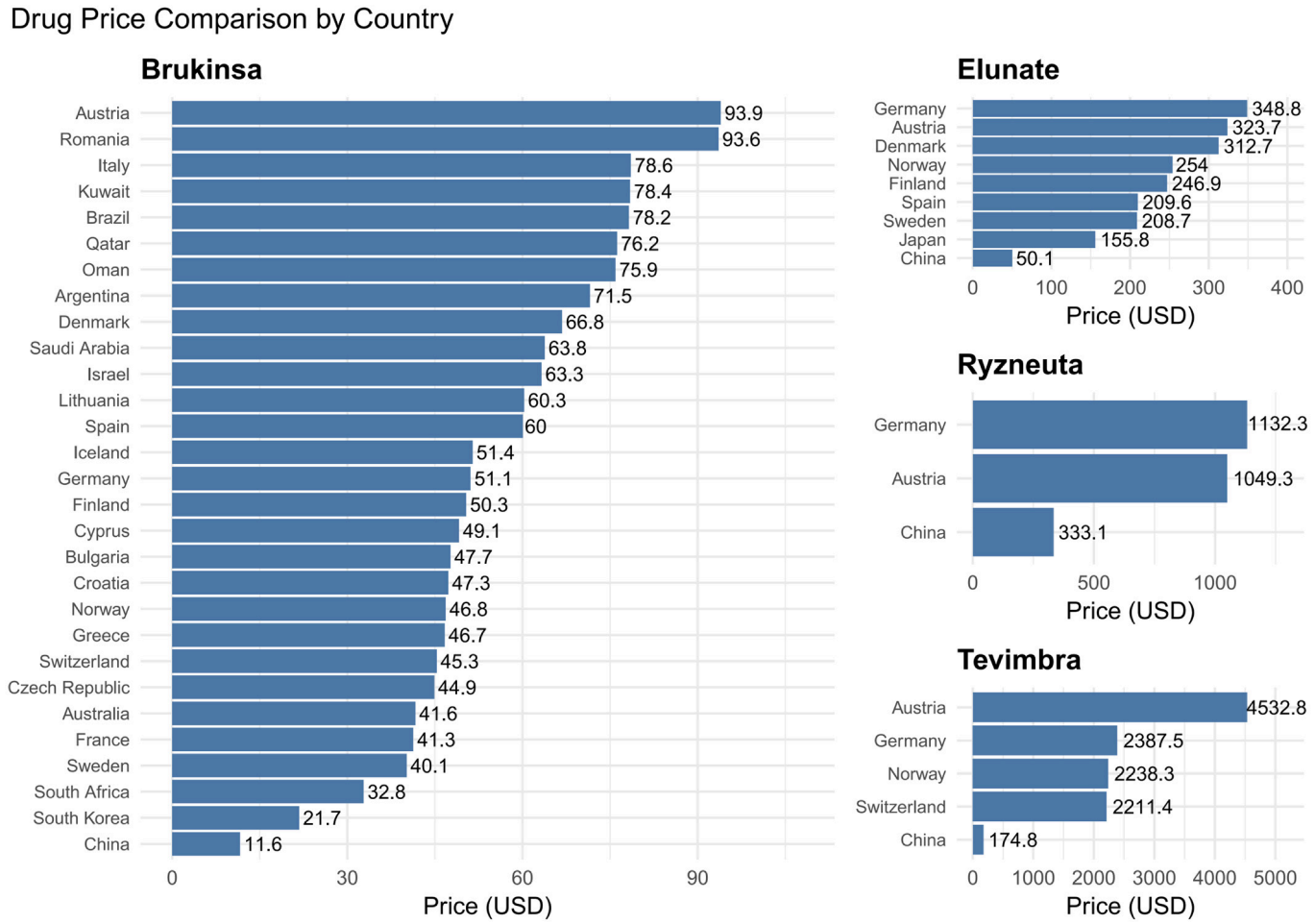


Figure 1. Public unit prices of selected Chinese-origin oncology medicines across observed markets (USD). Source: authors' analysis of public-price data from official government databases or government-recognised sources; analytical date 26 November 2024. Prices are expressed in US dollars at market exchange rates and exclude undisclosed rebates. Country coverage varies by medicine.

As a separate US benchmark, a manufacturer-sponsored 2024 budget-impact study reported an undiscounted zanubrutinib WAC of US $15,066 per package, using RED BOOK accessed on 26 February 2024 [24]. The Chinese analysis yielded US $11.63 per dose unit. Package and dose-unit prices are not directly comparable, so no China-to-US ratio is calculated without matching strength, pack size and treatment duration. The WAC observation is from a different date and is not a net price or an additional observation in the main cross-sectional dataset.

Country coverage differed materially by product. The comparator analyses comprised 28 market observations for zanubrutinib, eight for fruquintinib, five for tislelizumab and three for efbemalenograstim alfa. The markets available for within-product price comparisons and comparator-matched analyses need not coincide. Public prices may also represent different distribution-chain levels. Consequently, the observed price spreads do not constitute a representative global net-price or revenue comparison.

4.3. PPP-Adjusted Price Comparisons

PPP conversion also placed China at a low observed price position for zanubrutinib, fruquintinib and tislelizumab (Figure 2). For example, the fruquintinib unit price was 98.74 international dollars in China, 252.09 in Japan and 475.18 in Germany; zanubrutinib was 22.90 in China and 189.78 in Brazil. These comparisons suggest that selected nominal differences are not solely exchange-rate effects. The PPP-adjusted ranking of efbemalenograstim alfa is not used to support a cross-product conclusion. PPP-adjusted prices contextualise general purchasing-power differences and do not measure insured patients' affordability or confidential net payments.

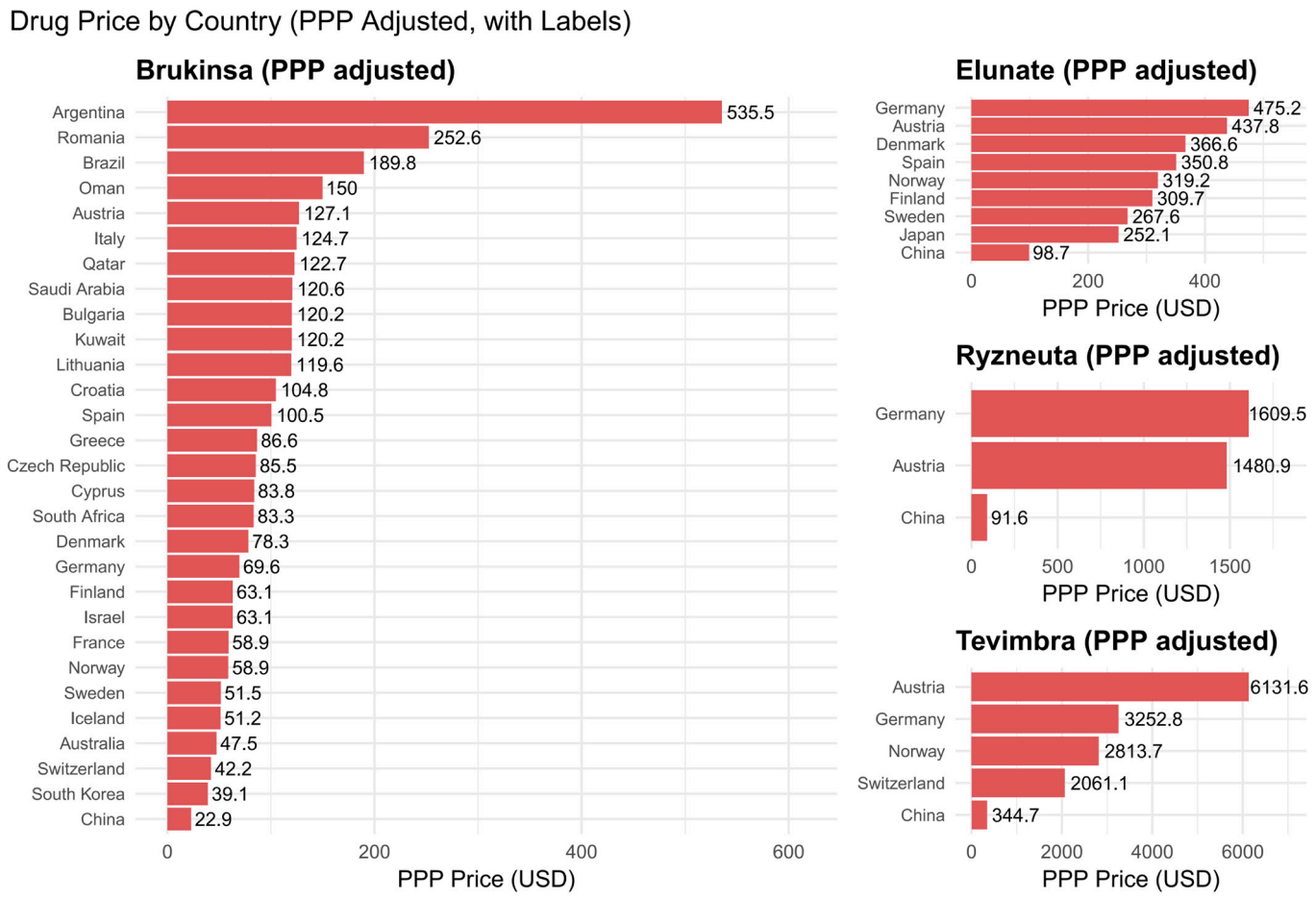


Figure 2. PPP-adjusted unit prices across observed markets. Source: authors' analysis of public prices using World Bank PPP conversion factors. PPP-adjusted values are expressed in international dollars; they are not transaction US-dollar prices. Country coverage varies by medicine.

4.4. Monthly Treatment-Cost Comparisons

The analysis yielded heterogeneous pair-specific median PPP-adjusted monthly acquisition costs (international dollars) (Figure 3): 10,155 for zanubrutinib vs. 10,421 for ibrutinib (matched-market n = 28); 6604 for fruquintinib vs. 36,514 for regorafenib (n = 8); 2814 for tislelizumab vs. 4927 for pembrolizumab (n = 5); and 1419 for efbemalenograstim alfa vs. 745 for pegfilgrastim (n = 3). The Chinese-origin medicine thus had a lower median in three pairs and a higher median in the supportive-care pair. These medians describe the observed market samples and should not be interpreted as indication-matched estimates of total treatment costs or cost-effectiveness.

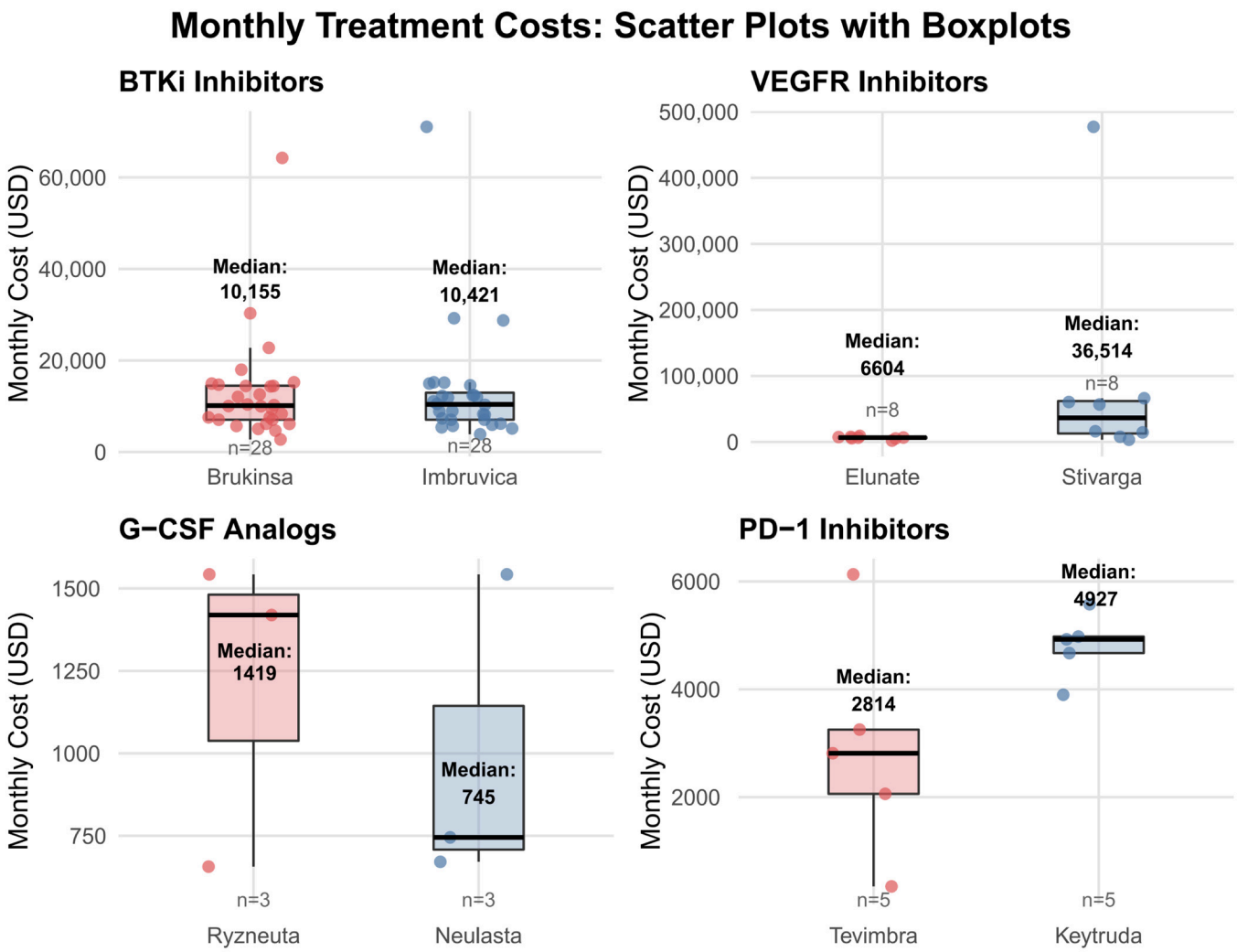


Figure 3. PPP-adjusted monthly treatment costs for Chinese-origin medicines and selected therapeutic comparators. Comparisons are descriptive; country sets and sample sizes differ by pair. Source: authors' public-price and labelled-dose calculations. Values are PPP-adjusted medicine acquisition costs, expressed in international dollars, and exclude other healthcare costs. Statistical summaries were generated using SPSS 26.0. Country coverage differs by pair; no pooled significance is inferred.

These findings do not establish a common treatment-class effect. Unequal country coverage, differing indications and dosing schedules, and the reversed supportive-care comparison preclude interpreting a pooled *p*-value as evidence of general clinical or economic undervaluation. No pooled inferential result is retained.

4.5. Evidence for a Home-Market Price Anchor

The nominal-price snapshot and regulatory chronology are consistent with potential exposure to a low origin-market price benchmark. Three products received their first approvals in China, whereas zanubrutinib received US approval first. However, approval is not commercial launch or reimbursement, and the timing of NRDL inclusion is not necessarily the timing of public disclosure of its payment standard. The chronology therefore identifies circumstances in which exposure might arise; it does not demonstrate when foreign payers observed or used the Chinese price.

The data do not show which foreign payer formally referenced China, whether an overseas price would have been higher in the absence of the Chinese price, or whether a

company delayed a launch because of ERP. Accordingly, the empirical finding is exposure to a low origin-market anchor rather than realised causal loss.

5. Discussion

5.1. Principal Findings

The four cases illustrate how an emerging originator market can also provide a low, observable public-price benchmark. The nominal-price analysis placed China lowest among the observed markets, while three products followed China-first regulatory pathways. These descriptive features motivate a price-reference hypothesis; they do not establish a realised home-market price penalty. PPP-adjusted comparisons should not be conflated with commercial reference prices.

The findings support the existence of a visible low-price anchor but not the stronger claim that the medicines were clinically undervalued. Price, clinical value and social value are distinct constructs. Demonstrating undervaluation would require indication-matched comparative benefit, quality-adjusted survival, cost offsets and a stated willingness-to-pay rule. Similarly, demonstrating harm to innovation would require longitudinal evidence on research investment, expected returns or pipeline decisions.

5.2. Why the Origin-Country Configuration Matters

An origin market may provide early patient access, clinical experience and an observable price benchmark during international expansion. A domestic reimbursement concession might then become negotiating information elsewhere if a relevant transmission route exists. The magnitude and even the presence of that effect depend on disclosure, foreign pricing rules, competing treatments, clinical evidence and negotiating context; none is identified causally by the cross-sectional comparisons.

Regulatory order alone is insufficient to establish exposure. Zanubrutinib was approved first in the United States, whereas fruquintinib and tislelizumab had longer intervals between Chinese and major Western approvals. Efbemalenograstim alfa expanded more rapidly. Dated reimbursement and price-disclosure records, together with foreign decision dates, are needed to determine whether the Chinese price was observable at the relevant negotiation.

5.3. Implications for Company Strategy

Multi-territory licensing contracts can address potential cross-market pricing issues through explicit governance, rather than presuming that confidential contracting eliminates ERP. First, define domestic reimbursement payments, international supply or transfer prices, local public list prices and net realised prices separately. A domestic NRDL payment standard need not automatically set an export supply price or royalty base. Second, establish a joint pricing committee with defined notification and consultation procedures for reimbursement submissions and material price changes, preserving each party's lawful decision rights and timely patient access.

Third, the parties can consider a negotiated minimum supply or transfer-price provision, accompanied by a review mechanism if a mandatory payer decision makes the territory commercially unviable. Such a floor governs the partners' commercial relationship; it cannot bind a regulator or prevent a payer from consulting a Chinese price. Fourth, avoid automatic most-favoured-price linkage to domestic NRDL terms by defining territories, products, price types and any exceptions to cross-territory adjustment clauses. Fifth, confidentiality, permitted-disclosure, audit and dispute-resolution provisions should address regulatory disclosure duties and the allocation of documented cross-market consequences. None of these provisions demonstrates a treatment effect or guarantees protection from

ERP. Their design requires jurisdiction-specific legal assessment and should not mandate anticompetitive resale prices or postpone clinically needed access. Confidential rebates and outcomes-based agreements remain options only where legally and operationally feasible.

5.4. Implications for Chinese Reimbursement Policy

China's reimbursement negotiations should consider manufacturers' international market returns alongside domestic patient access, clinical value and the sustainability of the health insurance fund. For medicines undergoing global expansion, potential interactions between domestic reimbursement arrangements and overseas pricing negotiations warrant attention. However, NRDL inclusion alone does not establish that a negotiated payment standard is publicly observable or has influenced foreign prices; existing rules already protect certain negotiated standards from public disclosure [3].

One policy option is to explore a clearer distinction between the insurance payment standard, publicly observable market prices, and manufacturers' net receipts. Where legally and operationally feasible, an affordable insurance payment standard could be combined with confidential rebates, price–volume arrangements or outcomes-based agreements tailored to the domestic reimbursement context. Such arrangements could potentially support domestic access while allowing differentiated pricing across markets. Their effectiveness would nevertheless depend on which prices remain observable throughout procurement and dispensing, whether foreign payers reference those prices, and how any differences affect patient cost sharing. Policy design should therefore safeguard affordability and equitable access, avoid shifting additional costs to patients, and apply transparent eligibility criteria without nationality-based preferential treatment. These options warrant further evaluation; their effects on international pricing and returns were not established by this study.

5.5. Implications for External Reference Pricing

For importing countries, the analysis illustrates why a listed price should not be treated as a context-free measure of fair value. The Chinese price may embody a negotiated exchange for national coverage and substantial expected volume. Transferring that price without transferring the associated volume, coverage obligations, or health-system context can undermine differential pricing. WHO recommends that ERP be used with other pricing tools and that reference-country selection follow explicit criteria. Reference systems should additionally consider income, coverage, confidential discounts, launch maturity, and whether the observed price is part of a price-volume agreement.

5.6. Strengths and Limitations

The study addresses an increasingly relevant but underexamined direction of pharmaceutical price spillover and combines price position with regulatory and reimbursement sequence. The cases cover different modalities and launch pathways, allowing analytical comparison rather than reliance on a single flagship product. Separating nominal from PPP-adjusted prices also avoids conflating commercial price exposure with affordability.

Several limitations remain. The four purposive cases cannot establish prevalence among Chinese-origin medicines. The study used official or government-recognised public benchmarks and omits confidential rebates; public prices are not harmonised net manufacturer receipts. US WAC is provided only as contextual information, so the study is not a complete global price or revenue comparison. Country coverage is unbalanced, and within-product and comparator-matched market sets may differ. The cross-figure consistency of the efbemalenograstim alfa PPP estimates limits interpretation of its adjusted price ranking. The single price snapshot cannot establish changes around NRDL entry or the first date

of public disclosure. Comparator populations and dosing assumptions are imperfectly aligned; acquisition costs omit other healthcare costs, and no comparative-efficacy synthesis or cost-effectiveness model was performed. PPP adjustment does not measure insured patients' out-of-pocket burden. Finally, the study lacks payer-level reference baskets, negotiation dossiers, observed launch decisions, and confidential transaction data, and cannot identify causal price, revenue, or innovation effects.

Future research should construct a longitudinal medicine-country panel containing launch application, approval, reimbursement, list price, estimated net price, ERP rules, and sales. A difference-in-differences or event-study design could test whether NRDL entry changes prices or launch hazards in markets that reference China, compared with markets that do not. Interviews with global pricing teams and payers could then identify the mechanism linking observable prices to launch and contracting decisions.

6. Conclusions

The four cases describe a configuration in which Chinese-origin oncology medicines expand internationally while relatively low domestic public-price observations are available. This motivates investigation of home-market price-reference exposure. Formal or informal transmission to foreign negotiations remains a hypothesis, requiring evidence on actual disclosure, payer rules, and decision timing.

The analysis does not establish that a low Chinese price caused foreign price reductions, launch delay, clinical undervaluation, or reduced innovation. Preserving affordable access while evaluating legitimate differential-pricing and contracting options requires better data on price types, reimbursement implementation and cross-market negotiating practices.

Author Contributions: Conceptualization, Z.M.; Methodology, Z.M.; Software, Z.M.; Validation, H.Y.; Investigation, Z.M. and W.H.; Resources, Z.M., H.Y. and W.H.; Data curation, Z.M., H.Y. and W.H.; Writing—original draft, Z.M. and Y.L.; Writing—review & editing, Z.M. and Y.L.; Supervision, Y.L.; Project administration, Y.L.; Funding acquisition, Y.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Ethical approval was not required because the study used publicly available aggregate data.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

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