Tyra Exploratory GCEA Societal Value Analysis — Technical Documentation

Dabogratinib (TYRA-300)

Indication: FGFR3-Altered, Low-Grade, Intermediate-Risk NMIBC (LG IR-NMIBC)

Scenario Analysis Framework (Version date: October 28, 2026)

This document presents the Generalized Cost-Effectiveness Analysis (GCEA) framework for dabogratinib (TYRA-300) in FGFR3-altered LG IR-NMIBC, structured as a scenario analysis: rather than anchoring on a single efficacy prediction, the analysis estimates the societal value implications of two long-term complete-response (CR) performance cases — Conservative (80%) and Optimistic (90%), set based on investor expectations — showing what each, if achieved and durably maintained, would imply for value.

Structure of the report:

- 1. Analytic Approach — methodology, comparator selection, scenario framework, and evidentiary framing
- 2. Indication & Population Definition
- 3. Value Elements In Scope (with preliminary calculator results)
- 4. Detailed Input Derivation — derivation, citations, and per-scenario input values for every element
- 5. References

1. Analytic Approach

1.1 Overview

This analysis covers a single indication for a Phase 2 asset. SURF302, dabogratinib's Phase 2 study in FGFR3-altered LG IR-NMIBC, is a single-arm, open-label, dose-optimization study; it does not include a randomized comparator arm. Two features of this evidentiary position shape the analytic approach:

- **No internal comparator arm exists.** Any comparator-arm data come from external natural-history and real-world sources — an unanchored comparison rather than a randomized head-to-head.
- **Efficacy evidence is early.** Initial SURF302 results (September 2026) established clinical proof of concept for selective oral FGFR3 inhibition and identified 60 mg once daily as the dose supporting the planned registrational adjuvant strategy. Rather than converting early, small-sample results into a single point prediction, this analysis is deliberately structured as a scenario framework (Section 1.4): it quantifies the value implication of a range of CR levels and is designed to be updated as landmark response and durability data mature.

1.2 Comparator Arm

Selected comparator: TURBT ± single perioperative chemotherapy dose (transurethral resection of the bladder tumor, with or without a single postoperative intravesical chemotherapy instillation).

Rationale:

- Matches the adjuvant (post-resection) setting of the planned Phase 3 development strategy.
- Represents the dominant real-world pathway for LG IR-NMIBC. Registry data show that immediate perioperative intravesical chemotherapy is delivered in only a small minority of TURBT cases in US

practice: 2.6% in an NSQIP analysis and 3.1% on average in the AQUA Registry (2015–2020, rising from 0.9% to 6.5%). Approximately 70% of patients with LG IR-NMIBC receive no adjuvant therapy intended to reduce recurrence at all. The comparator arm therefore reflects a real-world standard of care dominated by resection and surveillance.

- Has an available natural-history anchor (Section 1.3) drawn from the same source cited in SURF302 scientific conference presentations.

Comparators considered and not selected: BCG maintenance (reserved for high-risk NMIBC; not representative of the intermediate-risk population targeted here); emerging intravesical/device-based options (not yet standard of care, with insufficient real-world data to construct a comparator input set).

Key methodological principle: because the comparator represents real-world standard of care rather than a curated trial arm, every comparator-side input (e.g., recurrence rates, healthcare resource utilization, costs, QoL) should be sourced from real-world evidence wherever possible. Where only trial-derived or clinician-elicited data exist, this is flagged explicitly as a limitation and area for future extension.

1.3 Natural History Anchor

Confirmed anchor: Matulewicz & Steinberg, Rev Urol 2020 — cited in SURF302 scientific conference posters (ASCO-GU 2026, EAU 2026, AUA 2026).

- 60% of patients are disease-free at 24 months under standard of care; 40% have recurred by 24 months.
- Up to 30% of IR-NMIBC recurs within 1 year; up to 40% within 2 years.

Cross-check references retained for sensitivity purposes include SWOG S0337 (35% recurrence at 4 years with perioperative gemcitabine vs. 47% with saline) and published TURBT-only decay curves. Corroboration: TYRA-cited natural history (recurrence in up to 75% of patients within three years) annualizes to approximately 37% per year under a constant hazard — independently consistent with the 40%/year convention used throughout this framework.

Annualization and population calibration: published windows annualize differently because recurrence hazard declines with time from the last event: the 24-month anchor properly annualizes to ~22.5%/year, a 5-year FGFR3+ fit to ~27.5%/year, and the 3-year figure to ~37%/year.

The constant 40%/year convention carried throughout this framework therefore sits at the top of the all-comers range and is explicitly calibrated to the treated population — patients selected for persistently recurring disease (multifocal and/or large-lesion risk strata), whose per-patient hazard remains at or above this level — rather than to the all-comers FGFR3+ pool.

1.4 Scenario Framework — CR-Based Scenario Analysis

The treatment arm is constructed from the comparator anchor through a complete-response bridge. Under the framework's central assumption — a complete response achieved and durably maintained through the 24-month anchor window, with non-responders tracking the standard-of-care curve — the treatment-arm disease-free proportion is:

$$S(\text{treatment}, 24\text{mo}) = S(\text{comparator}, 24\text{mo}) + [1 - S(\text{comparator}, 24\text{mo})] \times CR = 0.60 + 0.40 \times CR$$

Under this construction, the assumed CR rate is mathematically identical to the relative reduction in recurrence. Two cases are carried throughout this document, labeled Conservative (80% CR) and Optimistic (90% CR). The labels refer to the range of investor expectations for the therapy's long-term performance, not

to the existing available evidence base: both cases sit above the Phase 2 landmarks observed to date (see below).

They are illustrative what-if cases — they price the value implication of each CR level and make no claim about which level will be achieved in the long run.

	Conservative	Optimistic
Assumed CR (durably maintained)	80%	90%
Disease-free at 24 months	92%	96%
Annual recurrence rate (treatment arm)	8%	4%
Implied hazard ratio vs. comparator	0.16	0.08
Relative reduction in recurrence	80%	90%

Orientation to observed data: SURF302's initial 3-month complete response landmarks at the go-forward 60 mg dose were 57% in the combined population (8/14) and 63% in the single-marker-lesion population (5/8), with best overall response CR rates of 64% and 75% respectively. Both cases carried here sit above these observed landmarks. They are carried as long-term performance cases on the thesis — held by the investors — that response deepens with continued oral dosing: one 3-month partial response had converted to complete response by 6 months at data cutoff, all 3-month CRs with 6-month assessments remained in response, and the first participant remained in CR at 12 months on continued treatment. The cases are therefore statements of potential, not readings of current data. Response durability at scale remains the framework's key open assumption.

Constant-multiplier simplification: each scenario's relative reduction is applied as a single, constant multiplier against the lifetime differential between the two arms, since we use the NPLB calculator to conduct back-of-envelope calculation. The NPLB calculator currently requires constant (non-time-varying) annual inputs. This is a documented simplifying assumption.

Update path: as SURF302 data mature, the framework updates in pre-specified stages: the 6-month landmark CR rate replaces the 3-month rate as the reference point when it reads out at scale (crediting later conversions and debiting early relapses); duration-of-response and recurrence-free-survival data then progressively replace the durability assumption itself.

1.5 Evidentiary Caveats

Three caveats apply throughout and are carried into every downstream section:

- **(a) Scenario analysis, not prediction.** The scenarios quantify value conditional on performance levels; which level materializes is an empirical question for the maturing SURF302 dataset and the planned Phase 3 program.
- **(b) Efficacy-effectiveness gap.** Trial endpoints as defined in protocol might not fully represent how recurrence is detected and managed in community practice. The durable-response bridge assumption in Section 1.4 additionally converts a landmark response measure into a time-to-event framework; this conversion is the analysis's most consequential structural assumption.

- **(c) Value-sourcing hierarchy.** For every input, the search order is: (i) a value measured directly in this disease and population; (ii) if unavailable, the closest available analog, clearly flagged as a substitution at the point of use.

Every input is tier-labeled: Observed (measured directly in a relevant population), Anchored (verified figure from an adjacent population or framework), or Premise (explicit modeling assumption).

1.6 Adherence and Delivery

A defining feature of this treatment landscape is that evidence-based adjuvant therapy is rarely delivered: the logistics of instillation-based care (e.g., same-day drug availability, trained personnel, hazardous-materials handling, repeated catheterization) and patient preference for less invasive treatments suppress real-world delivery to the single-digit percentages documented in Section 1.2.

An oral therapy prescribed at the point of care is structurally exempt from these barriers. This analysis treats that advantage in two distinct ways: (i) it is already embedded in the comparator arm, whose inputs reflect the weighted average of real-world care, in which the recurrence and cost anchors describe a largely untreated population, so the per-patient differential already prices the delivery failure as a population-average impact; and (ii) for the active treatment arm, 100% of patients are assumed to receive dabogratinib, with full persistence (Section 4.8). No separate per-patient adherence multiplier is applied.

1.7 Population Age & Model Horizon

The average age of the current prevalent LG IR-NMIBC population is set at 70 years, implying a model horizon of 30 years. This reflects the average age of patients currently living with the disease and is appropriate for a lifetime societal value model of the population as encountered in practice.

Verified disease-specific sources supporting 70 as a central estimate: Villegas et al. 2025, J Urol (n=521 primary TaLG NMIBC, median age 67.0); a low-risk NMIBC retrospective cohort (n=100, median 73); the SEER-Medicare low-grade Ta cohort (n=13,054, median 76; Medicare-linked and therefore upward-biased); and the ATLAS Phase 3 trial in LG IR-NMIBC (median 67–68 by arm).

2. Indication & Population Definition

2.1 Disease Definition

Indication: FGFR3-altered, low-grade, intermediate-risk non-muscle invasive bladder cancer (LG IR-NMIBC). Per AUA 2024 criteria, intermediate-risk NMIBC is defined by any of: recurrence within 1 year of low-grade Ta disease; solitary low-grade Ta tumor >3 cm; multifocal low-grade Ta; or low-grade T1. FGFR3 alterations (activating mutations or fusions) are present in an estimated 70–80% of IR-NMIBC tumors, making this the dominant molecular subtype within the risk category. The analysis is scoped to this FGFR3-altered population, mirroring SURF302 eligibility.

2.2 Population Sizing

- Approximately 20,000 patients per year in the US are newly diagnosed with FGFR3-altered intermediate-risk NMIBC; with a prevalence period of roughly 13 years, about 260,000 people are living with the disease (internal population framework, October 2026; tier: Anchored, pending independent epidemiological re-derivation).

- Of these, approximately 55,000 are on therapy at launch (the starting stock of persistently recurring patients), with about 15,000 new treatment starters per year thereafter and a steady-state stock of roughly 45,000–55,000 on therapy at any time; approximately 195,000 remain under active surveillance without therapy and enter the analysis through the peace-of-mind element (Section 4.11).
- For context: low-grade NMIBC represents approximately half of the ~82,000 incident US bladder cancer cases annually, with prevalent disease approaching 800,000 cases nationally.

2.3 Demographic Profile

Average age 70 (Section 1.7); male predominance of roughly 73–77% across disease-specific cohorts (Villegas et al. 2025: 73%; low-risk NMIBC cohort: 77%).

2.4 Disease Burden Profile

This is a morbidity-dominant, not mortality-dominant, disease. In the Villegas et al. 2025 cohort (n=521 primary TaLG NMIBC, median follow-up 9.6 years), 67% of patients recurred at least once, while 11% progressed in stage, 4% developed metastases, and 3% died of bladder cancer at a median of 9.6 years.

For the low-grade papillary population at intermediate risk of recurrence specifically, the overall risk of stage progression is 1–5% at 1 and 5 years (EAU guideline figure, as adopted in the ATLAS trial protocol), and FGFR3-mutant tumors are associated with genetically stable disease and favorable prognosis.

The clinical objective is therefore to reduce recurrence and its downstream procedural burden — not to extend survival. The societal value case flows through avoided procedures, preserved quality of life, and preserved productivity.

3. Value Elements In Scope

The following value flower petals are in scope, reflecting the disease profile in Section 2:

Petal	In Scope?	Rationale
Life years gained	Yes	Zero life-expectancy benefit assumed in all scenarios (affirmative conservatism; Section 4.1)
QoL gained	Yes	Two components: chronic non-recurrence vs. recurrence utility differential; procedure-specific disutility overlay
Medical cost savings	Yes	Recurrence reduction proportionally reduces recurrence-attributable cost (real-world claims), plus an incorporated 50% treatment-arm monitoring reduction (Premise; Section 4.3)
Productivity	Yes	Real-world WPAI data available; population-scaling caveats documented (Section 4.4)
Family / caregiver spillover	Yes	Three components: episodic procedure care, surveillance accompaniment, and chronic recurrence-state caregiving (Section 4.5)
Direct non-medical costs	Yes	TURBT-related travel burden (Section 4.6)
Peace of mind for the monitored population	Aggregate layer	Anticipatory (peace-of-mind) premium for monitored, untreated patients; excluded from per-patient treated values (Section 4.11)
Adherence	Yes	Delivery advantage embedded in comparator anchors and the 100% treatment-arm uptake assumption; no per-patient multiplier (Sections 1.6, 4.8)

Preliminary Findings

Results from the GCEA calculator under the current specification, reported at zero drug cost so that the per-patient figure is the gross discounted societal value per treated patient (net monetary benefit excluding drug acquisition cost).

Per treated patient (lifetime, discounted at 2%)

	Conservative (CR 80%)	Optimistic (CR 90%)
Lifetime discounted societal value per treated patient	$650,153	$714,574

Population inputs used for aggregation

Input	Value	Basis
Prevalent FGFR3-altered IR-NMIBC pool (US)	~260,000	~20,000 incident/yr × ~13-year prevalence; internal population framework (Oct 2026)
Starting stock of treated patients at launch (bolus, year 0)	55,000	Patients on therapy at launch; internal framework (updated 10/22/2026)
New treatment starters per year (years 1–69 / 1–99)	15,000	Internal framework; with ~3-year treatment duration, steady-state stock on therapy ≈ 45,000–55,000
Patients on therapy at any time (steady state)	~45,000–55,000	Implied by 15,000 starters/yr × ~3-year duration plus the declining launch stock
Monitored IR/HR patients not on therapy (peace-of-mind layer)	195,000	Internal framework
Discount rate; horizon	2%	GCEA Best Practice Guide
Peace-of-mind premium; valuation	0.02 QALY/yr per monitored person; $150,000/QALY	Section 4.11 (Premise; bracket 0.001–0.023)

Aggregate societal value (discounted at 2%)

	Conservative 70 cohorts	Optimistic 70 cohorts	Conservative 100 cohorts	Optimistic 100 cohorts
Treated patients (per-patient value × patient-equivalents)	$399.0B	$438.6B	$454.7B	$499.8B
Peace of mind, monitored population (195,000 × 0.02 × $150K × factor)	$22.4B	$22.4B	$25.7B	$25.7B
Total societal value	$421.4B	$460.9B	$480.4B	$525.5B

Note: The table presents the aggregate societal value for 70 cohorts and 100 cohorts (prevalent cohort with a size of 55,000 patients, and 69 (or 99) future incident cohorts with each incident cohort sized at 15,000. For individuals in each cohort, the discounted lifetime benefits are assumed to be the same. The societal benefits are discounted at 2% discount rate.

4. Detailed Input Derivation

Each subsection applies the scenario framework from Section 1.4 and the real-world-data principle from Section 1.2, organized in four parts: how the input is derived, key rationale (tagged as literature, government/administered data, or judgment call), resulting per-scenario input values, and outstanding issues. Every input is tier-labeled (Observed / Anchored / Premise).

Overview of Inputs by Scenario

The table below summarizes every quantified input, by arm and by scenario, in the order of the detailed derivations that follow. The comparator arm is identical across scenarios by construction.

Input	Comparator	Conservative (CR 80%)	Optimistic (CR 90%)
Life expectancy (yrs) — 4.1	15.20	15.20	15.20
Avg annual QoL utility — 4.2 (Spec A)	0.72049	0.82730	0.83590
Medical cost ($/yr) — 4.3	$114,524	$90,466	$87,631
Work hours lost (hrs/yr) — 4.4	134.7	27.6	14.4
Caregiver time (hrs/yr) — 4.5	35.34	8.78	5.36
Caregiver QoL gain — 4.5	—	+0.02	+0.02
Non-medical cost ($/yr) — 4.6	$44.83	$19.82	$18.95

4.1 Life Expectancy / Survival

How derived: all scenarios assume zero direct survival benefit; both arms carry 15.20 years (SSA 2023 Period Life Table, age 70).

Key rationale — judgment call, affirmatively conservative: the population-specific evidence argues the effect would be small in any case: stage progression in low-grade papillary IR-NMIBC is 1–5% at 5 years, FGFR3-mutant tumors carry favorable prognosis, and disease-specific mortality in the Villegas cohort was 0.31%/year. The zero-survival assumption is therefore a cited conservatism, not an omission.

Tier: Anchored (life table); Premise (zero-differential scope decision).

4.2 Quality of Life

Structured in two additive parts plus a combined total: (A) a chronic background utility differential between disease-free and recurrence states, (B) a procedure and administration disutility overlay covering TURBT episodes, monitoring procedure, and comparator pathway's instillation-based adjuvant therapy, and (c) fear-of-recurrence relief term is added in the treatment arm.

4.2.A Chronic Background Utility Differential

How derived: a weighted average of two health-state utility anchors, using each arm's disease-free/recurrence split. Non-recurrence utility 0.824 (Jiang et al. 2021, US EQ-5D-5L population norm, ages 65–74); recurrence utility 0.781 (Cooper et al. 2023, TTO-elicited, BCG-unresponsive NMIBC — a more severe population, used as the closest available anchor; both are cross-population analogs, flagged per Section 1.5(c)). Tier: Anchored/Premise.

	Comparator	Conservative	Optimistic
Disease-free / recurred split	60% / 40%	92% / 8%	96% / 4%
Chronic utility (4.2.A)	0.80680	0.82056	0.82228

4.2.B Procedure and Administration Disutility Overlay

How derived: disutility from four procedure-incurred components (i.e., TURBT episodes, surveillance cystoscopy, perioperative single-dose chemotherapy and adjuvant intravesical course), each scaled by the relevant event rate.

The procedure-disutility values are based on published NMIBC economic models (Zhang et al. 2013, per Kulkarni et al.): 0.025 QALYs per cystoscopy and 0.03 per TURBT, applied consistently to both arms — surveillance cystoscopy at the observed 3.0 visits/year in the comparator and 1.5 visits/year in the treatment arm (the same 50% reduction carried in the medical-cost line), and TURBT at each arm's episode rate.

Note: in the treatment arm, oral dabogratinib is itself the adjuvant therapy, replacing instillation-based administration and its associated burden. This displacement is a core element of the oral therapy's value proposition. Any salvage intravesical therapy following oral-therapy failure is not separately modeled and would modestly offset this line; the treatment arm's own administration and tolerability burden is tracked separately (Section 4.8 and the pending adverse-event refinement).

Tier: Anchored (published model values; Kulkarni plausible range 0.003–0.05 per cystoscopy).

Component	Comparator	Conservative	Optimistic
TURBT episodes (0.03/episode)	0.01080	0.00216	0.00108
Surveillance cystoscopy (0.025/visit)	0.07500	0.03750	0.03750
Adjuvant courses + perioperative dose	0.00051	—	—
Combined (chronic and procedure layer)	0.72049	0.78090	0.78370

4.2.C Fear-of-Recurrence State Decrement

How derived: fear of cancer recurrence (FCR) is a measured health-state burden distinct from procedure disutility: in long-term cancer survivors, EQ-5D utility with clinically significant FCR was 0.887 versus 0.945 without — a 0.058 decrement (Anchored).

The main specification treats the full decrement as applying to all comparator patients (100%), on the reasoning that the modeled comparator population is the persistently recurring subset under intensive surveillance (3.0 cystoscopies/year), for whom the recurrence threat is continuous and realized; the comparator's chronic utility anchors are taken to embed this surveillance-state burden.

Relief is credited to the treatment arm as a utility uplift of 0.058 × (1 − treatment recurrence rate ÷ comparator recurrence rate), i.e., proportional to the reduction in recurrence risk; the framework claims no intervention effect on fear itself. Resulting treatment-arm utilities (lie within the general US adult EQ-5D-5L range (age-matched 65–74 norm of 0.824).

Combined (chronic and procedure layer)	0.72049	0.78090	0.78370

FCR state term	Comparator	Conservative	Optimistic
FCR relief uplift to treatment arm (0.058 × CR)	—	+0.0464	+0.0522
Differential contribution (main)	—	+0.0464	+0.0522

4.2.C Combined QALY Values (Main Specification — Specification A + FCR term)

	Comparator	Conservative	Optimistic
Average annual utility	0.72049	0.82730	0.83590
Annual differential vs. comparator	—	+0.10681	+0.11541

Outstanding issues: no value in this section was measured directly in the FGFR3-altered LG IR-NMIBC population; a population-specific utility elicitation (e.g., TTO or DCE covering the recurrence and surveillance experience) would upgrade this element and is recommended as an evidence-generation priority.

The costs of intravesical administration are already contained in the claims-based figures of Section 4.3, so components (ii) and (iii) are quality-of-life lines only; the adverse-event burden of intravesical therapy (dysuria, chemical cystitis) beyond the administration decrement is not yet separately quantified and would add conservatively to the comparator side.

4.3 Medical Cost Savings

How derived: a bottom-up construction from real-world claims, with four components carried in the main specification: the observed recurrence-year increment, an intermediate-risk increment premium, an explicit progression term, and the monitoring-reduction component. Each arm's annual cost equals a common base disease-management cost plus these components at the arm's event rates.

Primary source — Observed: Bree et al. 2022 (JAMA Network Open; SEER-Medicare, n=13,054 low-grade Ta patients, 2004–2013): median annual costs $76,669 with recurrence versus $53,909 without — an observed recurrence-year increment of $22,760 in study dollars, claims-defined by receipt of a subsequent TURBT.

Inflation to 2026 USD: BLS Medical Care CPI. The main specification carries the pooled-study-period reading of the Bree dollar-year (chain ×1.58), giving an increment of $35,961 and a base level of $85,176 in 2026 USD; full-text confirmation of the dollar-year remains pending, and the conservative 2013-dollar chain (×1.396; increment $31,771) is retained as the first reversion below.

Currency status: all cost inputs in this framework are expressed in 2026 USD — unit prices (cystoscopy fee schedule, cytology, imaging, mileage) are current 2026 administered or list prices, and study-sourced figures are inflated on the stated chains.

Intermediate-risk increment premium: a 30% premium is applied to the all-LG-Ta increment ($35,961 → $46,749). Anchor: Medicare prices TURBT by tumor size, and the intermediate-risk definition (>3 cm; multifocal) maps onto the higher-priced codes — across every 2026 Medicare payment system, a large-tumor resection (CPT 52240) pays 52–61% more than a small one (52234), and medium (52235) pays 16–18% more;

large resections map to a separate, higher hospital outpatient APC. Multifocal cases additionally permit separate-lesion billing, and AUA surveillance intensity within recurrence-years is itself risk-tiered.

Decomposition: the size-mix uplift applies to the TURBT-episode share of the increment (~25–35% of the recurrence-year delta; +20–60% for the IR size mix → +5 to +21% on the increment), plus the risk-tiered surveillance share (+4 to +10%), plus multifocality admission effects — a supported range of ~15–30%, with 30% carried at the top of that range (modeling decision 10/21/2026); 15% and 25% are the sensitivity ends (main differentials ~$17.0–$25.0K and ~$17.8–$25.9K respectively, before the monitoring component).

Tier: Anchored structure (Observed fee ratios) × Premise weights (IR size mix; TURBT share of increment).

2026 Medicare TURBT payment by tumor size	Small 52234 (0.5–2 cm)	Medium 52235 (2–5 cm)	Large 52240 (>5 cm)	Large vs. small
Physician fee	$217	$255	$344	+59%
ASC facility	$502	$584	$799	+59%
Hospital outpatient (APC)	APC 5374: $3,601	APC 5374: $3,601	APC 5375: $5,478	+52%

Mean-versus-median adjustment: Bree et al. report median costs; economic evaluation values expected (mean) costs, and healthcare cost distributions are right-skewed, with means typically 1.2–1.5× medians and the skew concentrated in high-utilization (recurrence) years. A 1.3× adjustment is applied to the recurrence-year increment ($46,749 → $60,774) pending the reported means from the Bree full text, which would replace the multiplier with an observed figure. Tier: Anchored principle / Premise magnitude.

Payer-mix adjustment: the treated population is not exclusively Medicare fee-for-service; with an assumed ~25% commercially insured share at ~2× Medicare rates, a blended 1.25× multiplier is applied to the Medicare-derived components (recurrence increment and progression term). It is not applied to the monitoring component, which is already priced at commercial rates.

Effective recurrence-year increment: $60,774 × 1.25 = $75,967. Tier: Premise (payer-mix share); Anchored (rate ratio range).

Progression term: an explicit progression-cost line at a 0.8%/year comparator progression rate × $200,000 per event (anchored to SEER-Medicare incremental costs of progressed bladder cancer: ~$172,000 cumulative for long-term survivors plus first-year regional-stage incremental costs of ~$42,000) × 0.5 mediation of the treatment effect, with the payer-mix multiplier applied. Tier: Anchored per-event magnitude; Premise rate and mediation.

Monitoring-reduction component: the treatment arm's cystoscopic monitoring requirement is assumed reduced by 50%, priced at commercial rates — $1,380/year subtracted from the treatment arm (pool derivation below; two-leg duration rationale: ctDNA-informed monitoring during treatment, guideline-earned de-escalation under durable disease-free status thereafter). Gross of replacement-assay cost (dollar-for-dollar offset); a demographically blended rate (~1.25×) would yield +$860/year.

Monitoring cost pool, bottom-up (per comparator-patient-year, Medicare): surveillance visits at the observed real-world intensity of 3.0 cystoscopies/year (Bree et al. 2022, median — adopted over the guideline-implied 2.40 per the real-world principle) × a facility-mix-blended per-visit cost of ~$459 (cystoscopy: 50% office at $216, 25% ASC at $381, 25% hospital outpatient at $783 — 2026 Medicare national averages; mix is a Premise — plus urine cytology, CPT 88112, carried at $60, range $35–150, exact MPFS rate pending) = $1,377/year, plus annualized upper-tract imaging (~$500 CT urography every 2 years =

$250/year, Premise), for a gross pool of ~$1,630/year. Netting the portion already embedded in the Bree recurrence-year increment (~$250, Premise apportionment) gives an addable pool of $1,380/year at Medicare rates; commercial rates are applied as a 2.0× multiplier (observed contract dispersion ~1.1–2.5×; Premise), giving $2,760/year.

Cross-check — model-based reference: *Mossanen et al. 2019 (Markov model of guideline-concordant care, EORTC risk strata) yields a 5-year intermediate-risk total of $146,250 in 2017 USD (≈$182,600 in 2026 USD, ×1.2485). Retained as a reference only: its composition is dominated (~81%) by progression at EORTC-intermediate rates well above this low-grade population's observed 0.4–5%.*

Component (2026 $)	Comparator	Conservative	Optimistic
TURBT-recurrence-years/yr	0.360	0.072	0.036
Base level (common; cancels)	$85,176	$85,176	$85,176
Recurrence increment × rate ($75,967/recurrence-yr, effective)	$27,348	$5,470	$2,735
Progression term	$2,000	$1,200	$1,100
Monitoring reduction (treatment arm)	—	−$1,380	−$1,380
Annual medical cost (2026$)	$114,524	$90,466	$87,631
Annual cost differential	—	$24,058	$26,893

Tier summary: Observed (Bree increment); Anchored (inflation methodology; fee-schedule unit prices); Premise (pooled dollar-year pending confirmation; IR premium weights; mean/median multiplier pending Bree means; payer-mix share; progression rate and mediation; 90% conversion; monitoring component); the IR premium structure itself is Anchored to Medicare size-stratified fee ratios.

Population comparability: the Bree cohort spans all low-grade Ta disease, including the low-risk majority; this analysis's intermediate-risk, FGFR3-altered population recurs more (handled by sourcing recurrence rates from IR-specific evidence) and the IR increment premium above addresses the per-episode cost difference. The 2004–2013 care era is additionally flagged; inflation adjustment does not capture practice-pattern drift.

4.4 Productivity

How derived: WPAI-measured overall work productivity loss (59.0%; Totev et al. 2024, N=171 US NMIBC patients, N=77 employed), applied across a full year for anyone recurring that year (state-based framing), scaled by a 27% employment rate (BLS labor-force participation, ages 65–74, matching the age-70 population) and each arm's recurrence rate.

Output expressed in hours and valued at the $43/hour wage rate per the GCEA Calculator default. Per the main-specification composition, surveillance-visit market time is included in both arms (2.75 hrs/visit × 27% employment × 3.0 comparator / 1.5 treatment visits per year); non-market visit time remains excluded pending the valuation-convention decision.

Population caveat: the Totev sample comprises intravesically treated patients (83% BCG), a more treatment-intensive population than TURBT-managed LG IR-NMIBC; the 59% impairment figure may therefore overstate per-recurrence productivity loss here.

Tier: Anchored (WPAI magnitude); Premise (employment-rate match, state-based framing, wage rate).

	Comparator	Conservative	Optimistic
Work hours lost/yr	132.5	26.5	13.3

4.5 Caregiver Burden

How derived: three additive time components.

(a) Episodic procedure care: 12 hours per TURBT episode (6 hours acute, days 1–2; 6 hours recovery tail, days 3–14), using colonoscopy as the closest procedural analog adjusted for TURBT's greater invasiveness and catheter-care needs (60% of TURBT patients are discharged with a catheter; Deacon et al. 2024), scaled by the 90% TURBT-conversion rate and each arm's recurrence rate.

(b) Surveillance accompaniment: expected annual surveillance cystoscopies from the AUA/SUO guideline schedule (intensity resets to every 3–6 months for two years after a recurrence, de-escalating with sustained disease-free status), multiplied by a 70% accompaniment rate and 2.75 hours per accompanied visit including transport and waiting.

(c) Chronic recurrence-state caregiving: an incremental 66 informal caregiving hours per year for patients in a recurrence year, anchored to observed partner-caregiver time in localized prostate cancer during the active-management year (Li et al.; mean 65.9 caregiving hrs/yr, with a further 76.2 hrs/yr of household chores conservatively excluded) — a population analog matched on age, sex distribution, spousal caregiving structure, and urologic disease management. Component (c) attaches to recurrence status rather than TURBT conversion, since the caregiving state outlasts the procedure itself.

Tiers: (a) Premise (double analog). (b) Observed visit schedule (AUA/SUO) with Premise accompaniment parameters. (c) Observed in localized prostate cancer; Anchored analog here, with the population mapping stated explicitly.

Caregiver fear-of-recurrence is documented (~48% report clinically significant levels; Webb et al. 2023), a +0.02 annual caregiver quality-of-life gain is carried in the treatment arm

Component (hrs/yr)	Comparator	Conservative	Optimistic
(a) Episodic TURBT care	4.32	0.86	0.43
(b) Surveillance accompaniment	4.62	2.64	2.29
(c) Chronic recurrence-state care	26.40	5.28	2.64
Total caregiver hours/yr	35.34	8.78	5.36

Guards and notes: caregiver travel is not separately counted (the caregiver shares the vehicle trip costed in Section 4.6); caregiver hours are valued once, as time cost, with no separate caregiver work-absence line; the valuation rate for predominantly spousal caregivers around age 70 (market wage vs. replacement cost) is a flagged methodological choice.

4.6 Direct Non-Medical Costs

How derived: a per-visit travel/parking cost — (30-mile round trip × $0.235 IRS medical mileage rate, effective July 2026) + $5 parking = $12.05/visit — with 2 visits per TURBT episode ($24.10/episode), scaled by the 90% conversion rate and each arm's recurrence rate. The 30-mile distance derives from the access statistic that >87% of Medicare NMIBC patients live more than 30 minutes from a urologist.

Per the main-specification composition, surveillance-visit travel is included in both arms at the same per-visit cost (3.0 comparator / 1.5 treatment visits per year).

Tier: Anchored (IRS rate); Premise (distance derivation, visit counts).

	Comparator	Conservative	Optimistic
Non-medical cost ($/yr)	$8.68	$1.74	$0.87

4.7 Dynamics

How derived: dabogratinib is a small-molecule, FGFR3-selective tyrosine kinase inhibitor administered as chronic once-daily oral therapy; small molecules typically face substantial generic price decline at loss of exclusivity. Dynamics do not impact our calculation as we are estimating the total societal benefits that the therapy bring to the treated patient (independent of the cost of the therapy).

Future incident cohorts are considered consistent with Section 2.2's population sizing; the cohort growth rate remains unsourced. Discounting: 2% (QALYs) / 2% (costs.

Tier: Anchored (classification, discounting, GRACE); Premise (exclusivity horizon, price decline).

4.8 Adherence and Persistence

Consistent with Section 1.6, no per-patient adherence multiplier is applied in any scenario. The comparator-side delivery failure is already embedded in the real-world comparator anchors; applying a separate multiplier would double-count.

On the treatment side, real-world persistence on chronic oral therapy is the relevant parameter; initial SURF302 tolerability results (no treatment-related discontinuations or dose reductions at 60 mg; most adverse events Grade 1–2) are directionally supportive but not yet sufficient to quantify a persistence input. This remains a flagged refinement for future rounds as longer-duration exposure data accumulate.

4.9 Consolidated Input Specification

The table below consolidates every resolved input. Fields not yet resolved are marked Pending rather than populated with placeholder values.

Input	Comparator	Conservative	Optimistic
Life expectancy (yrs)	15.20	15.20	15.20
Average annual QoL utility	0.72049	0.82730	0.83590
Medical cost (2026 $/yr)	$114,524	$90,466	$87,631
Work hours lost (hrs/yr)	134.7	27.6	14.4
Wage rate ($/hr)	$43	$43	$43
Caregiver time (hrs/yr)	35.34	8.78	5.36

Input	Comparator	Conservative	Optimistic
Caregiver QoL gain (treatment arm)	—	+0.02	+0.02
Non-medical cost ($/yr)	$44.83	$19.82	$18.95
Discount rates (QALY/cost)	2% / 2%	2% / 2%	2% / 2%

4.10 Value Drivers Readers Can Test

This specification carries a number of explicit modeling choices alongside its observed and anchored inputs. Rather than a fixed set of sensitivity analyses, the drivers below are the ones a reader is most likely to want to vary, with the direction and approximate magnitude of each. Reference values for the conservative end of each driver are retained in the relevant derivation sections.

- Efficacy and durability (the central assumption)
- Monitoring reduction for cystoscopic monitoring.
- Procedure-disutility scale
- Fear-of-recurrence term (prevalence and placement)
- Caregiver quality-of-life gain
- Peace-of-mind premium for the monitored population
- Survival

4.11 Peace of Mind for the Monitored Population

Concept: patients under active surveillance who are not on therapy still gain from the existence of a non-invasive treatment option: the prospect of recurrence becomes less frightening when recurrence no longer implies the invasive pathway. This is the anticipatory ("peace of mind") value. The closest product analogy is needle-free epinephrine, whose societal value has been publicly framed (including by NPLB) as residing substantially in the reassurance of carrying it rather than in deployment. This element applies at the aggregation layer only (monitored population × premium × horizon) and does not enter the per-patient treated inputs or NMB.

Annual premium per monitored person	Basis	Aggregate (195K monitored, $150K/QALY)	70-year discounted (factor 38.25)
0.02 (carried value)	Daily-anxiety value referenced from the needle-free epinephrine analysis (internal reference; citation pending)	$585M/yr	~$22.4B

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