	Cost containment of global monoclonal antibody drugs and cancer clinical trials via LLM focused reasoning
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	Traceability Part C TRC Human-in-the-Loop Verification, Scope = Financial Verifications of ChatGPT o3-mini.
	The content is available under CC BY 4.0. Refer to manuscript Table 2 for article references. (Pages 1-8)
	Generation C1: Four Page Report on 30 "Clinical mAb Cancer Cost" Summaries
	Executive Summary
	3.5 Sonnet 30 Clinical Summaries
1	- ABC therapy had an incremental cost-effectiveness ratio (ICER) of "$193,926.48/QALY" over a 20-year horizon
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	For instance, analyses of atezolizumab plus bevacizumab with chemotherapy for cervical cancer reported ICERs of "$193,926.48/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
2	- The incremental cost-effectiveness ratio (ICER) was "$73,601.43" per QALY, exceeding China's willingness-to-pay threshold of "$39,855.79"
	o3-mini LLM Author and Quote
	"Cai H. et al. 2024"
	"$73,601.43/QALY" (reported by "Cai H. et al. 2024"), both exceeding local thresholds.
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
3	Using Markov modeling, the authors found that while BEV+LOM improved progression-free survival, the incremental cost-effectiveness ratio (ICER) of "$84,071.12" per quality-adjusted life year (QALY) exceeded China's willingness-to-pay threshold of "$35,906" per QALY
	o3-mini LLM Author and Quote
	"Chen Z. et al. 2024"
	Similar challenges have been observed with bevacizumab combinations in glioblastoma and metastatic colorectal cancer, where ICERs of "$84,071.12/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
4	- The resulting incremental cost-effectiveness ratio (ICER) was "$188,904.09" per QALY gained, substantially exceeding China's willingness-to-pay threshold of "$38,201" per QALY
	o3-mini LLM Author and Quote
	"Li Y. et al. 2024"
	and "$188,904.09/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
5	- Resulting incremental cost-effectiveness ratio (ICER) was "$114,275.67" per QALY
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	(e.g., "$114,275.67/QALY" for pembrolizumab combinations in cervical cancer
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
6	- This exceeded the US willingness-to-pay threshold of "$150,000/QALY"
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	ICERs exceeding "$150,000/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
7	- Price reduction of 29.81% needed in China for cost-effectiveness
	o3-mini LLM Author and Quote
	"Xiang G. et al. 2024"
	In markets such as China, evaluations of nivolumab and other PD-1 inhibitors often require reductions ranging from 29.81%

Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
8	- Current pricing requires a 72.1% reduction in nivolumab costs to reach cost-effectiveness thresholds
	o3-mini LLM Author and Quote
	"Meng K. et al. 2024"
	to 72.1% to meet local cost-effectiveness thresholds
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
9	- Modest 40-46% price reductions seen in European markets like Germany and Poland for biosimilars
	o3-mini LLM Author and Quote
	(Broer L. et al. 2024)
	typically between 40% and 46% in European contexts
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
10	- Total pharmaceutical cost avoidance of "$92,662,609" over the 10-year period
	o3-mini LLM Author and Quote
	"Carreras M. et al. 2024"
	(with total avoided costs reaching "$92,662,609" over 10 years
Y	**In-Context**
	Technical Details
	3.5 Sonnet 30 Clinical Summaries
11	- 20-year lifetime horizon analysis
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	Models ranged from 5-year to lifetime horizons with cycle lengths varying from 1 week to 3 weeks (e.g., a 20-year horizon
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
12	- 10-year Markov model with 21-day cycles
	o3-mini LLM Author and Quote
	"Peng J. et al. 2024"
	and a 10-year horizon
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
13	- Atezolizumab per cycle: "$10,072.20"
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	For example, atezolizumab was priced at "$10,072.20" per cycle
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
14	- Bevacizumab per cycle: "$8,617.84"
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	while bevacizumab costs varied from "$8,617.84" per cycle
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
15	- Bevacizumab: "$222.88" per 100mg
	o3-mini LLM Author and Quote
	"Li Y. et al. 2024"
	to "$222.88" per 100mg
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
16	Lin Y. et al. 2024 Pembrolizumab: "$2,458" per 100mg
	o3-mini LLM Author and Quote
	"Lang W. et al. 2025"

	pembrolizumab at "$2,458" per 100mg
P	**Partial-Context, Incorrect Author**
	3.5 Sonnet 30 Clinical Summaries
17	- Sintilimab: "$160.57" per 100mg
	o3-mini LLM Author and Quote
	"Xiang Z. et al. 2024"
	sintilimab at "$160.57" per 100mg
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
18	- Pembrolizumab shows modest survival benefits (0.09 QALYs)
	o3-mini LLM Author and Quote
	"Nie J. et al. 2024"
	Incremental QALY gains ranged from modest increases of 0.09 QALYs
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
19	This report analyzes the cost-effectiveness of adding atezolizumab (a monoclonal antibody) to standard bevacizumab plus chemotherapy (ABC therapy) compared to bevacizumab plus chemotherapy alone (BC therapy)
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	Several studies compared mAb-based combination therapies to standard chemotherapy
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
20	This report analyzes the cost-effectiveness of combining pembrolizumab (a PD-1 targeting monoclonal antibody) with chemotherapy versus chemotherapy alone
	o3-mini LLM Author and Quote
	"Lang W. et al. 2025"
	Several studies compared mAb-based combination therapies to standard chemotherapy
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
21	This report analyzes the cost-effectiveness of nivolumab plus ipilimumab compared to the EXTREME regimen (cetuximab + cisplatin/carboplatin + fluorouracil)
	o3-mini LLM Author and Quote
	"Ye D. et al. 2024"
	nivolumab plus ipilimumab vs. EXTREME regimen
Y	**In-Context**
	Key Insights
	3.5 Sonnet 30 Clinical Summaries
22	- ABC therapy had an incremental cost-effectiveness ratio (ICER) of "$193,926.48/QALY" over a 20-year horizon
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	the addition of atezolizumab in cervical cancer resulted in an ICER of "$193,926.48/QALY"
Y	**In-Context, In 30 Reports**
	3.5 Sonnet 30 Clinical Summaries
23	Sensitivity analyses revealed:
	o3-mini LLM Author and Quote
	"Cai H. et al. 2024"
	Sensitivity analyses in several studies
Y	**In-Context, In 30 Reports**
	3.5 Sonnet 30 Clinical Summaries
24	- One-way sensitivity analysis identifies nivolumab cost as key driver
	o3-mini LLM Author and Quote
	"Meng K. et al. 2024"
	Sensitivity analyses in several studies
Y	**In-Context, In 30 Reports**
	3.5 Sonnet 30 Clinical Summaries
25	- Current pricing requires a 72.1% reduction in nivolumab costs to reach cost-effectiveness thresholds

	o3-mini LLM Author and Quote
	"Meng K. et al. 2024")
	nivolumab's cost requires a reduction of up to 72.1%
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
26	- Modest 40-46% price reductions seen in European markets like Germany and Poland for biosimilars
	o3-mini LLM Author and Quote
	(Broer L. et al. 2024)
	where modest price reductions (40–46%) were insufficient to meet cost-effectiveness thresholds, reinforcing the need for innovative pricing strategies
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
27	- Incremental cost: "$18,199.63"
	o3-mini LLM Author and Quote
	"Lang W. et al. 2025"
	increased total treatment costs by "$18,199.63" with an additional 0.23 QALYs
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
28	- EV: "$131.52" per mg - Reducing EV price to "$20" per mg would achieve 50% probability of cost-effectiveness -The incremental cost was "$962,240.8" per patient - The incremental cost-effectiveness ratio (ICER) was "$558,973" per QALY
	o3-mini LLM Author and Quote
	"Li A. et al. 2024"
	enfortumab vedotin plus pembrolizumab incurred an incremental cost of "$962,240.8" per patient and an ICER of "$558,973/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
29	showed an incremental cost-effectiveness ratio (ICER) of "$25,239.29" per quality-adjusted life year (QALY)
	o3-mini LLM Author and Quote
	"Xiang Z. et al. 2024"
	demonstrated favorable cost-effectiveness with an ICER of "$25,239.29/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
30	- Total pharmaceutical cost avoidance of "$92,662,609" over the 10-year period
	o3-mini LLM Author and Quote
	"Carreras M. et al. 2024"
	with total avoided costs reaching "$92,662,609" over a 10-year period.
Y	**In-Context**
	<u>Generation C2: Financial Solutions to 30 "Clinical mAb Cancer Cost" Summaries</u>
	3.5 Sonnet 30 Clinical Summaries
31	- A 10% reduction in atezolizumab price would make ABC therapy cost-effective at "$121,531.24/QALY"
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	For atezolizumab-based combinations in cervical cancer, a "10% reduction" lowers the ICER to "$121,531.24/QALY"
Y	**In-Context, In 30 Reports**
	3.5 Sonnet 30 Clinical Summaries
32	- Price reduction of 38% (to "$1,764" per 1,200mg) would be needed for atezolizumab to achieve cost-effectiveness
	o3-mini LLM Author and Quote
	"Cai H. et al. 2024"
	while in the Chinese setting a "38% reduction" is required
Y	**In-Context, In 30 Reports**
	3.5 Sonnet 30 Clinical Summaries
33	China requires 29.81% nivolumab price reduction (to "$920.87/100mg") for cost-effectiveness
	o3-mini LLM Author and Quote
	"Xiang G. et al. 2024"
	For nivolumab plus chemotherapy in advanced urothelial carcinoma, a "29.81% reduction" (to "$920.87/100mg") is necessary for costeffectiveness in China
Y	**In-Context**

	3.5 Sonnet 30 Clinical Summaries
34	- Current pricing requires a 72.1% reduction in nivolumab costs to reach cost-effectiveness thresholds
	o3-mini LLM Author and Quote
	"Meng K. et al. 2024"
	in other settings up to "72.1%" reduction is indicated
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
35	- EV: "$131.52" per mg - Reducing EV price to "$20" per mg would achieve 50% probability of cost-effectiveness
	o3-mini LLM Author and Quote
	"Li A. et al. 2024"
	enfortumab vedotin; for example, achieving cost-effectiveness may require reducing its price to "$20" per mg from "$131.52" per mg
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
36	However, targeted price adjustments for patients with PD-L1 Combined Positive Score (CPS) ≥10 could potentially improve both therapeutic and economic outcomes. This report analyzes the cost-effectiveness of combining pembrolizumab (a PD-1 targeting monoclonal antibody) with chemotherapy versus chemotherapy alone
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024" and "Lang W. et al. 2025"
	For example, targeting patients with PD-L1 Combined Positive Scores ≥10—where cost-effectiveness improves—can be part of a value-based strategy
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
37	- Modest 40-46% price reductions seen in European markets like Germany and Poland for biosimilars
	o3-mini LLM Author and Quote
	(Broer L. et al. 2024)
	Although current biosimilar price reductions (around 40–46%) have shown only modest savings
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
38	- Even with biosimilar versions, bevacizumab would need a 60.75% price reduction from "$222.88" to "$87.49" per 100mg to become cost-effective
	o3-mini LLM Author and Quote
	"Li Y. et al. 2024"
	even biosimilar versions required a "60.75%" reduction to become cost-effective
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
39	- Patient subgroups with high PD-L1 expression showed better cost-effectiveness with nivolumab plus ipilimumab -The analysis suggests serplulimab plus chemotherapy represents a financially viable first-line treatment option for PD-L1 positive ESCC patients in China - Remains cost-effective across PD-L1 expression levels, unlike some competitor treatments
	o3-mini LLM Author and Quote
	"Ye D. et al. 2024", "Li J. et al. 2024", and "Xiang Z. et al. 2024"
	studies have shown better economic outcomes in patients with high PD-L1 expression or favorable performance status
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
40	- Total pharmaceutical cost avoidance of "$92,662,609" over the 10-year period
	o3-mini LLM Author and Quote
	"Carreras M. et al. 2024"
	One analysis reported total avoided drug costs of "$92,662,609" over 10 years due to trial sponsorship
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
41	Sensitivity Analysis Results: - Annual discount rate most impactful on ICER
	o3-mini LLM Author and Quote
	"Gan Y. et al. 2024"
	Sensitivity analyses indicate that the length of treatment has a substantial impact on total cost, suggesting that optimizing the duration without compromising efficacy can improve economic outcomes
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
42	showed an incremental cost-effectiveness ratio (ICER) of "$25,239.29" per quality-adjusted life year (QALY)
	o3-mini LLM Author and Quote
	"Xiang Z. et al. 2024"

	sintilimab plus chemotherapy, with an ICER of "$25,239.29/QALY"
Y	**In-Context**
	Generation C3: Table of Solutions to 30 "Clinical mAb Cancer Cost" Summaries
	3.5 Sonnet 30 Clinical Summaries
43	- A 10% reduction in atezolizumab price would make ABC therapy cost-effective at "$121,531.24/QALY"
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	Lowers ICER to "$121,531.24/QALY" "10% reduction"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
44	- Price reduction of 38% (to "$1,764" per 1,200mg) would be needed for atezolizumab to achieve cost-effectiveness
	o3-mini LLM Author and Quote
	"Cai H. et al. 2024"
	"38% reduction"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
45	- Price reduction of 29.81% needed in China for cost-effectiveness - Current pricing requires a 72.1% reduction in nivolumab costs to reach cost-effectiveness thresholds
	o3-mini LLM Author and Quote
	"Xiang G. et al. 2024" and "Meng K. et al. 2024"
	"29.81% reduction" (with up to "72.1%" reduction in alternative analysis)
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
46	- EV: "$131.52" per mg - Reducing EV price to "$20" per mg would achieve 50% probability of cost-effectiveness
	o3-mini LLM Author and Quote
	"Li A. et al. 2024"
	Reduce price to "$20 per mg" From current price of "$131.52 per mg"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
47	However, targeted price adjustments for patients with PD-L1 Combined Positive Score (CPS) ≥10 could potentially improve both therapeutic and economic outcomes. This report analyzes the cost-effectiveness of combining pembrolizumab (a PD-1 targeting monoclonal antibody) with chemotherapy versus chemotherapy alone
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024" and "Lang W. et al. 2025"
	Implement managed entry agreements and risk-sharing arrangements; target patients with PD-L1 CPS ≥10 -Improves cost-effectiveness in subgroups
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
48	- Even with biosimilar versions, bevacizumab would need a 60.75% price reduction from "$222.88" to "$87.49" per 100mg to become cost-effective
	o3-mini LLM Author and Quote
	"Li Y. et al. 2024"
	Promote the use of biosimilars for expensive mAbs such as bevacizumab -Achieve approximately "60.75% reduction" in price
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
49	- Patient subgroups with high PD-L1 expression showed better cost-effectiveness with nivolumab plus ipilimumab -The analysis suggests serplulimab plus chemotherapy represents a financially viable first-line treatment option for PD-L1 positive ESCC patients in China - Remains cost-effective across PD-L1 expression levels, unlike some competitor treatments
	o3-mini LLM Author and Quote
	"Ye D. et al. 2024", "Li J. et al. 2024", and "Xiang Z. et al. 2024"
	Target treatment to patients with high PD-L1 expression or favorable performance status -Demonstrates improved cost-effectiveness in these subgroups -Results in modest QALY gains and improved ICERs (e.g., incremental gains observed)
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
50	- Total pharmaceutical cost avoidance of "$92,662,609" over the 10-year period
	o3-mini LLM Author and Quote
	"Carreras M. et al. 2024"
	Expand clinical trial participation and philanthropic programs -Total cost avoidance of "$92,662,609" over 10 years
Y	**In-Context**

	3.5 Sonnet 30 Clinical Summaries
51	Sensitivity Analysis Results: - Annual discount rate most impactful on ICER
	o3-mini LLM Author and Quote
	"Gan Y. et al. 2024"
	Optimize treatment length -Sensitivity analyses show duration is a key cost driver
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
52	showed an incremental cost-effectiveness ratio (ICER) of "$25,239.29" per quality-adjusted life year (QALY)
	o3-mini LLM Author and Quote
	"Xiang Z. et al. 2024"
	Sintilimab plus chemotherapy achieved an ICER of "$25,239.29/QALY" -Observed ICER of "$25,239.29/QALY"
Y	**In-Context**
	Generation C4: Table of Forecasts to 30 "Clinical mAb Cancer Cost" Summaries
	3.5 Sonnet 30 Clinical Summaries
53	A 10% reduction in atezolizumab price would make ABC therapy cost-effective at "$121,531.24/QALY" AND - ABC therapy had an incremental cost-effectiveness ratio (ICER) of "$193,926.48/QALY" over a 20-year horizon
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024"
	Atezolizumab plus bevacizumab and chemotherapy"10% reduction" AND Lowers ICER to "$121,531.24/QALY" AND Baseline ICER of "$193,926.48/QALY"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
54	Price reduction of 38% (to "$1,764" per 1,200mg) would be needed for atezolizumab to achieve cost-effectiveness
	o3-mini LLM Author and Quote
	"Cai H. et al. 2024"
	Atezolizumab plus bevacizumab and chemotherapy "38% reduction" AND Achieves cost-effectiveness under local threshold
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
55	China requires 29.81% nivolumab price reduction (to "$920.87/100mg") for cost-effectiveness AND - Current pricing requires a 72.1% reduction in nivolumab costs to reach cost-effectiveness thresholds
	o3-mini LLM Author and Quote
	"Xiang G. et al. 2024" and "Meng K. et al. 2024"
	Nivolumab plus chemotherapy "29.81% reduction" (alternatively up to "72.1% reduction") AND Reduces nivolumab cost to "$920.87/100mg"
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
56	EV: "$131.52" per mg AND - Reducing EV price to "$20" per mg would achieve 50% probability of cost-effectiveness AND - The incremental cost was "$962,240.8" per patient AND - The incremental cost-effectiveness ratio (ICER) was "$558,973" per QALY
	o3-mini LLM Author and Quote
	"Li A. et al. 2024"
	Enfortumab vedotin plus pembrolizumab Reduce price to "$20 per mg" AND Required to achieve cost-effectiveness; current ICER remains "$558,973/QALY" AND Current price of "$131.52 per mg" must be reduced
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
57	Even with biosimilar versions, bevacizumab would need a 60.75% price reduction from "$222.88" to "$87.49" per 100mg to become cost-effective AND - The resulting incremental cost-effectiveness ratio (ICER) was "$188,904.09" per QALY gained, substantially exceeding China's willingness-to-pay threshold of "$38,201" per QALY
	o3-mini LLM Author and Quote
	"Li Y. et al. 2024"
	Bevacizumab AND Approximately "60.75% reduction" AND Baseline ICER remains high (e.g., "$188,904.09/QALY") without reduction
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
58	Even with charitable pricing discount of 41.4%, the ICER remained at "$52,765.69" per QALY AND - Resulting incremental cost-effectiveness ratio (ICER) was "$114,275.67" per QALY
	o3-mini LLM Author and Quote
	"Lin Y. et al. 2024" and "Lang W. et al. 2025"
	Pembrolizumab combination therapies AND With a "41.4% charitable pricing discount", ICER reduces to "$52,765.69/QALY" AND Baseline ICER of "$114,275.67/QALY" reduced through targeted pricing measures
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries

59	Total pharmaceutical cost avoidance of "$92,662,609" over the 10-year period
	o3-mini LLM Author and Quote
	"Carreras M. et al. 2024"
	Solid tumors across clinical trials AND Total drug cost avoidance of "$92,662,609" over 10 years
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
60	Sensitivity Analysis Results: AND - Annual discount rate most impactful on ICER
	o3-mini LLM Author and Quote
	"Gan Y. et al. 2024"
	Various cancer indications (e.g., mesothelioma, urothelial carcinoma) AND Sensitivity analyses show that shorter duration reduces overall treatment costs
Y	**In-Context**
	3.5 Sonnet 30 Clinical Summaries
61	showed an incremental cost-effectiveness ratio (ICER) of "$25,239.29" per quality-adjusted life year (QALY) AND - This ICER falls below China's willingness-to-pay threshold of "$38,223.34"
	o3-mini LLM Author and Quote
	"Xiang Z. et al. 2024"
	Advanced gastric cancer, China AND Achieved ICER of "$25,239.29/QALY" AND Favorable relative to local threshold of "$38,223.34/QALY"
Y	**In-Context**