Potential Decision Drivers for Positive Recommendations of New Cancer Therapies in the Brazilian Private Healthcare System: Analysis of Recent HTA Submissions

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Supplementary Materials:

- **Supplementary table 1.** Description of cancer pharmacological technologies appraisals by the Brazilian Private Healthcare System (October 2021 to December 2022) – Part I
- **Supplementary table 2.** Description of cancer pharmacological technologies appraisals by the Brazilian Private Healthcare System (October 2021 to December 2022) – Part II

Supplementary table 1. Description of cancer pharmacological technologies appraisals by the Brazilian Private Healthcare System (October 2021 to December 2022) – Part I

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Darolutamide (UAT 1)	Urologic	Nonmetastatic castration-resistant prostate cancer	Favorable	Favorable	Phase III RCT	NA	Yes	Yes	No
Regorafenib (UAT 3)	Digestive	Metastatic colorectal cancer	Negative	Negative	MA of Phase III RCT	Yes	Yes	Yes	Yes
Brigatinib (UAT 8)	Lung	First line treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) that is positive for anaplastic lymphoma kinase (ALK)	Favorable	Favorable	MA of Phase III RCT	Yes	Yes	No	No
Trifluridine + Tipiracil (UAT 9)	Digestive	Metastatic colorectal cancer previously treated with two prior systemic treatment regimens for advanced disease, i.e., third-line treatment.	Favorable	Favorable	MA of Phase III RCT	Yes	Yes	Yes	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Cabozantinib (UAT 10)	Hepatic	Monotherapy for the treatment of hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib tosylate.	Negative	Negative	Phase III. Indirect comparison with MAIC.	Yes	Yes	Yes	No
Trifluridine + Tipiracil (UAT 12)	Digestive	Third-line treatment of adult patients with metastatic gastric cancer including gastroesophageal junction adenocarcinoma.	Favorable	Favorable	Phase III RCT	No	Yes	Yes	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Erdafitinib (UAT 13)	Urologic	Treatment of adult patients with locally advanced or metastatic urothelial carcinoma, whose tumors have certain genetic alterations of fibroblast growth factor receptors (FGFR), who have disease progression during or after at least one previous line of chemotherapy, or for up to 12 months after neoadjuvant or adjuvant chemotherapy.	Negative	Negative	Phase II, single-arm. Indirect comparison with MAIC.	Yes	Yes	Yes	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Venetoclax (UAT 15)	Hematologic	First-line treatment of patients who have chronic lymphocytic leukemia in combination with obinutuzumab.	Favorable	Favorable	Phase III RCT	No	Yes	No	No
Apalutamide (UAT 11)	Urologic	Metastatic castration-sensitive prostate cancer (mcpsc)	Negative	Favorable	Phase III RCT	Yes	Yes	Yes	No
Acalabrutinib (UAT 16)	Hematologic	First-line treatment of chronic lymphocytic leukemia (CLL)	Favorable	Favorable	Phase III RCT. Indirect comparison (NMA and MAIC) not considered in the assessment.	Yes	Yes	No	No
Acalabrutinib (UAT 17)	Hematologic	Treatment of relapsed or refractory chronic lymphocytic leukemia (CLL)	Favorable	Favorable	Phase III RCT	No	Yes	No	No
Acalabrutinib (UAT 18)	Hematologic	Treatment of relapsed or refractory mantle	Negative	Favorable	Phase II, single-arm	Yes	Yes	No	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
		cell lymphoma (MCL)							
Enzalutamide (UAT 19)	Urologic	Metastatic castration-sensitive prostate cancer (mcpsc) without concomitant use of docetaxel	Negative	Favorable	Phase III RCT	Yes	Yes	Potentially yes (immature data)	No
Lorlatinib (UAT 20)	Lung	First-line treatment of patients with advanced non-small cell lung cancer (NSCLC) positive for anaplastic lymphoma kinase (ALK)	Favorable	Favorable	Phase III RCT	NA	Yes	Questionable (no gain versus relevant comparator)	No
Gilteritinib (UAT 23)	Hematologic	Relapsed or refractory acute myeloid leukemia (AML) with FLT3 gene mutation	Favorable	Favorable	Phase III RCT	No	NA	Yes	Yes
Lorlatinib (UAT 27)	Lung	ALK-positive non-small cell lung cancer, in second and later lines	Negative	Negative	Phase II, single-arm. Indirect	Yes	Yes	NA	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
					comparison with MAIC.				
Abemaciclib (UAT 28)	Breast	Early breast cancer with a high risk of recurrence, hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, and lymph node positive, in combination with endocrine therapy	Negative	Negative	Phase III RCT	Yes	Yes	No (immature data)	No
Olaparib (UAT 32)	Gynecologic	Relapsed, high-grade, BRCA-mutated, platinum-sensitive ovarian serous or endometrioid carcinoma.	Favorable	Favorable	Phase III RCT	Yes	Yes	Yes	No
Olaparib (UAT 33)	Gynecologic	Newly diagnosed, advanced, high-grade, platinum-sensitive, BRCA-	Favorable	Favorable	Phase III RCT	Yes	Yes	No	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
		mutated ovarian carcinoma.							
Regorafenib (UAT 47)	Digestive	Treatment of patients with advanced or metastatic colorectal cancer who have previously been treated with, or are not considered candidates for, available therapies. These include fluoropyrimidine-based chemotherapy, anti-VEGF therapy and anti-EGFR therapy.	Favorable	Favorable	Phase III RCT	Yes	Yes	Yes	No.

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Pembrolizumab + Axitinib (UAT 50)	Urologic	Metastatic or advanced clear cell renal cell carcinoma, not previously treated and with prognostic risk classified as intermediate or unfavorable in first line	Negative	Favorable	Phase III RCT	Yes	Yes	Questionable (no gain versus relevant comparator)	No
Niraparib (UAT 54)	Gynecologic	Advanced (stages III and IV – FIGO) high-grade ovarian, fallopian tube, or primary peritoneal carcinoma that have responded completely or in part after completion of first-line platinum-based chemotherapy in maintenance treatment	Favorable	Favorable	Phase III RCT	Yes	Yes	Potentially yes (immature data)	No

Technology (ID)	Type of cancer	Detailed indication	Preliminary recommendation	Final recommendation	Source for clinical benefit	Low/very low evidence certainty for eficacy outcomes	PFS increase or similar to comparators	Benefit in OS	Potential safety issues
Cabozantinib + Nivolumab (UAT 56)	Urologic	First-line advanced or metastatic renal cell carcinoma	Negative	Favorable	Phase III RCT	Yes	Yes	Questionable (no gain versus relevant comparator)	Not considered but higher SAE vs. compara otors

Legend: ID, identification; UAT, *Unidade de Análise Técnica* (Technical analysis unit); RCT, randomized controlled trial; MA: meta-analysis; PFS, progression-free survival; OS, overall survival.

Supplementary table 2. Description of cancer pharmacological technologies appraisals by the Brazilian Private Healthcare System (October 2021 to December 2022) – Part II

Technology (ID)	Type of cancer	Recommendations		Cost-effectiveness analysis	ICER above 3 GDP per capita*	Savings / neutral BI	External HTA agencies recommendations*		Public consultation	
		Preliminary	Final				Positive	Negative	Contributions	Concordance with preliminary recommendation
Darolutamide (UAT 1)	Urologic	Favorable	Favorable	Cost-utility	Yes	No	Yes	No	631	91%
Regorafenib (UAT 3)	Digestive	Negative	Negative	Cost-utility	Yes	No	No	Yes	593	3%
Brigatinib (UAT 8)	Lung	Favorable	Favorable	Cost-utility	Yes	No	Yes	No	39	95%
Trifluridine + Tipiracil (UAT 9)	Digestive	Favorable	Favorable	Cost-utility	Yes	No	Yes	Yes	349	98%
Cabozantinib (UAT 10)	Hepatic	Negative	Negative	Cost-utility	Yes	No	Yes	Yes	30	17%
Trifluridine + Tipiracil (UAT 12)	Digestive	Favorable	Favorable	Cost-utility	Yes	No	Yes	Yes	331	99%
Erdafitinib (UAT 13)	Urologic	Negative	Negative	Cost-utility	Yes	No	NA	NA	109	2%
Venetoclax (UAT 15)	Hematologic	Favorable	Favorable	Cost-minimization	No	Yes	Yes	No	90	96%
Apalutamide (UAT 11)	Urologic	Negative	Favorable	Cost-utility	Yes	No	Yes	No	562	0.7%
Acalabrutinib (UAT 16)	Hematologic	Favorable	Favorable	Cost-minimization	No	Yes	Yes	Yes	173	99%
Acalabrutinib (UAT 17)	Hematologic	Favorable	Favorable	Cost-minimization	No	Yes	Yes	No	149	99%
Acalabrutinib (UAT 18)	Hematologic	Negative	Favorable	Cost-minimization	No	Yes	Yes	No	194	0.5%

Technology (ID)	Type of cancer	Recommendations		Cost-effectiveness analysis	ICER above 3 GDP per capita*	Savings / neutral BI	External HTA agencies recommendations*		Public consultation	
		Preliminary	Final				Positive	Negative	Contributions	Concordance with preliminary recommendation
Enzalutamide (UAT 19)	Urologic	Negative	Favorable	Cost-utility	Yes	No	Yes	No	88	14%
Lorlatinib (UAT 20)	Lung	Favorable	Favorable	Cost-minimization	No	Yes	Yes	Yes	61	97%
Gilteritinib (UAT 23)	Hematologic	Favorable	Favorable	Cost-utility	Yes	No	Yes	No	54	96%
Lorlatinib (UAT 27)	Lung	Negative	Negative	Cost-utility	Yes	No	Yes	Yes	189	3.2%
Abemaciclib (UAT 28)	Breast	Negative	Negative	Cost-utility	Yes	No	No	Yes	420	1.7%
Olaparib (UAT 32)	Gynecologic	Favorable	Favorable	Cost-utility	No	No	Yes	No	1269	99.8%
Olaparib (UAT 33)	Gynecologic	Favorable	Favorable	Cost-utility	No	No	Yes	No	811	99.4%
Regorafenib (UAT 47)	Digestive	Favorable	Favorable	Cost-utility	Yes	Yes	No	Yes	404	98.8%
Pembrolizumab + Axitinib (UAT 50)	Urologic	Negative	Favorable	Cost-utility	Yes	No	Yes	Yes	146	3.4%
Niraparib (UAT 54)	Gynecologic	Favorable	Favorable	Cost-utility	Yes	No	Yes	No	1012	99.1%
Cabozantinib + Nivolumab (UAT 56)	Urologic	Negative	Favorable	Cost-utility	Yes	No	Yes	No	118	2.5%

Legend: ID, identification; UAT, *Unidade de Análise Técnica* (Technical analysis unit); RCT, randomized controlled trial; MA: meta-analysis; PFS, progression-free survival; OS, overall survival. *External HTA agencies included: NICE, IQWiG, CADTH, HAS, SMC, PBAC/PBS.