NOTA TÉCNICA 9719

IDENTIFICAÇÃO DA REQUISIÇÃO

CÂMARA/VARA:2ª Vara Cível

COMARCA: Belo Horizonte

I – DADOS COMPLEMENTARES À REQUISIÇÃO:

IDADE: 60 anos

PEDIDO DA AÇÃO: Pertuzumabe + Trastuzumabe + Anastrozol

DOENÇA(S) INFORMADA(S): C50

FINALIDADE / INDICAÇÃO: CARCINOMA DE MAMA

REGISTRO NO CONSELHO PROFISSIONAL: CRMMG-10736

NÚMERO DA SOLICITAÇÃO: 2026.0009719

II – PERGUNTAS DO JUÍZO:

1 - O tratamento é eficaz e recomendado para o caso da paciente?

2 - Há evidência científica do uso dos medicamentos para casos como o da paciente?

3- Há outro substituto terapêutico do medicamento para o caso da paciente, a exceção daqueles do qual já se valeu?

III – CONSIDERAÇÕES/RESPOSTAS:

Dados de Literatura (dados copilados)

A combinação de pertuzumabe + trastuzumabe + anastrozol é uma estratégia terapêutica utilizada no câncer de mama HER2-positivo e receptor hormonal (HR)-positivo, com aplicações tanto no cenário metastático quanto em contextos de de-escalonamento de quimioterapia. O contexto clínico determina como essa combinação se encaixa no tratamento.

Cenário Metastático (Doença Recorrente/Estádio IV)

O principal estudo que avaliou essa combinação é o PERTAIN (fase II, N=258), que randomizou pacientes com câncer de mama HER2+/HR+ metastático ou localmente avançado para pertuzumabe + trastuzumabe + inibidor de aromatase (anastrozol ou letrozol) versus trastuzumabe + inibidor de aromatase, com ou sem quimioterapia de indução. Na análise final (mediana de seguimento >6 anos), a adição de pertuzumabe resultou em SLP mediana de 20,6 vs. 15,8 meses (HR 0,67; P=0,006). O benefício foi potencialmente maior nos pacientes que não receberam quimioterapia de indução (26,6 vs. 12,5 meses). Não houve diferença significativa em sobrevida global (60,2 vs. 57,2 meses; HR 1,05; P=0,78). Clinical Cancer Research[1]

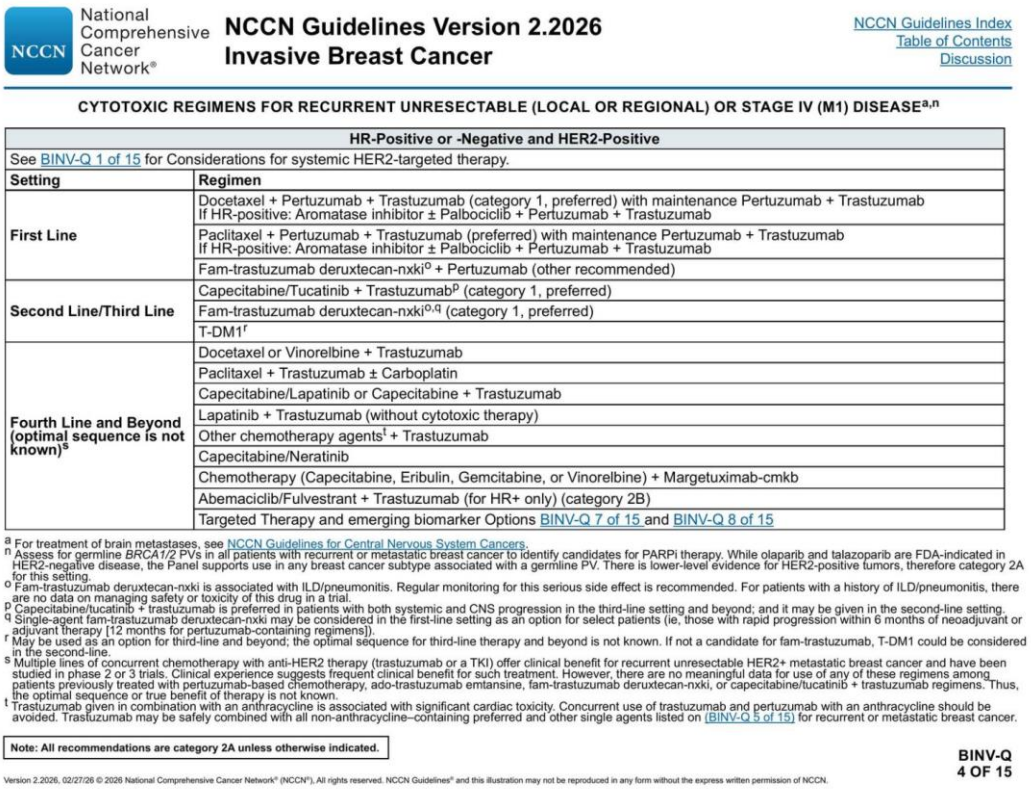
De acordo com as diretrizes NCCN (v2.2026), no cenário de primeira linha para doença metastática HER2+/HR+, as opções preferidas incluem taxano + pertuzumabe + trastuzumabe, com manutenção de pertuzumabe + trastuzumabe. Após a descontinuação da quimioterapia, inibidor de aromatase (± palbociclibe) pode ser adicionado ao pertuzumabe + trastuzumabe. NCCN[2] A combinação de inibidor de aromatase ± trastuzumabe (sem pertuzumabe) também é listada como "outra opção recomendada".

Cenário Neoadjuvante (De-escalonamento)

O estudo WSG-TP-II (fase II) avaliou terapia endócrina (incluindo anastrozol) + trastuzumabe + pertuzumabe versus paclitaxel + trastuzumabe + pertuzumabe no cenário neoadjuvante para câncer de mama HER2+/HR+ precoce. Embora a combinação sem quimioterapia tenha demonstrado atividade biológica (redução de Ki67), as taxas de resposta patológica completa foram inferiores ao braço com quimioterapia, e essa abordagem permanece investigacional. JAMA[3]

Posologia

- Pertuzumabe: dose de ataque 840 mg IV, manutenção 420 mg IV a cada 3 semanas
- Trastuzumabe: dose de ataque 8 mg/kg IV, manutenção 6 mg/kg IV a cada 3 semanas
- Anastrozol: 1 mg via oral diariamente



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CYTOTOXIC REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[a,n]

HR-Positive or -Negative and HER2-Positive	
See BINV-Q 1 of 15 for Considerations for systemic HER2-targeted therapy.	
Setting	**Regimen**
First Line	Docetaxel + Pertuzumab + Trastuzumab (category 1, preferred) with maintenance Pertuzumab + Trastuzumab If HR-positive: Aromatase inhibitor ± Palbociclib + Pertuzumab + Trastuzumab
	Paclitaxel + Pertuzumab + Trastuzumab (preferred) with maintenance Pertuzumab + Trastuzumab If HR-positive: Aromatase inhibitor ± Palbociclib + Pertuzumab + Trastuzumab
	Fam-trastuzumab deruxtecan-nxki[o] + Pertuzumab (other recommended)
Second Line/Third Line	Capecitabine/Tucatinib + Trastuzumab[p] (category 1, preferred)
	Fam-trastuzumab deruxtecan-nxki[o,q] (category 1, preferred)
	T-DM1[r]
Fourth Line and Beyond (optimal sequence is not known)[s]	Docetaxel or Vinorelbine + Trastuzumab
	Paclitaxel + Trastuzumab ± Carboplatin
	Capecitabine/Lapatinib or Capecitabine + Trastuzumab
	Lapatinib + Trastuzumab (without cytotoxic therapy)
	Other chemotherapy agents[t] + Trastuzumab
	Capecitabine/Neratinib
	Chemotherapy (Capecitabine, Eribulin, Gemcitabine, or Vinorelbine) + Margetuximab-cmkb
	Abemaciclib/Fulvestrant + Trastuzumab (for HR+ only) (category 2B)
	Targeted Therapy and emerging biomarker Options BINV-Q 7 of 15 and BINV-Q 8 of 15

[a] For treatment of brain metastases, see NCCN Guidelines for Central Nervous System Cancers.
[n] Assess for germline *BRCA1/2* PVs in all patients with recurrent or metastatic breast cancer to identify candidates for PARPi therapy. While olaparib and talazoparib are FDA-indicated in HER2-negative disease, the Panel supports use in any breast cancer subtype associated with a germline PV. There is lower-level evidence for HER2-positive tumors, therefore category 2A for this setting.
[o] Fam-trastuzumab deruxtecan-nxki is associated with ILD/pneumonitis. Regular monitoring for this serious side effect is recommended. For patients with a history of ILD/pneumonitis, there are no data on managing safety or toxicity of this drug in a trial.
[p] Capecitabine/tucatinib + trastuzumab is preferred in patients with both systemic and CNS progression in the third-line setting and beyond; and it may be given in the second-line setting.
[q] Single-agent fam-trastuzumab deruxtecan-nxki may be considered in the first-line setting as an option for select patients (ie, those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens]).
[r] May be used as an option for third-line and beyond; the optimal sequence for third-line therapy and beyond is not known. If not a candidate for fam-trastuzumab, T-DM1 could be considered in the second-line.
[s] Multiple lines of concurrent chemotherapy with anti-HER2 therapy (trastuzumab or a TKI) offer clinical benefit for recurrent unresectable HER2+ metastatic breast cancer and have been studied in phase 2 or 3 trials. Clinical experience suggests frequent clinical benefit for such treatment. However, there are no meaningful data for use of any of these regimens among patients previously treated with pertuzumab-based chemotherapy, ado-trastuzumab emtansine, fam-trastuzumab deruxtecan-nxki, or capecitabine/tucatinib + trastuzumab regimens. Thus, the optimal sequence or true benefit of therapy is not known.
[t] Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided. Trastuzumab may be safely combined with all non-anthracycline–containing preferred and other single agents listed on (BINV-Q 5 of 15) for recurrent or metastatic breast cancer.

Note: All recommendations are category 2A unless otherwise indicated.

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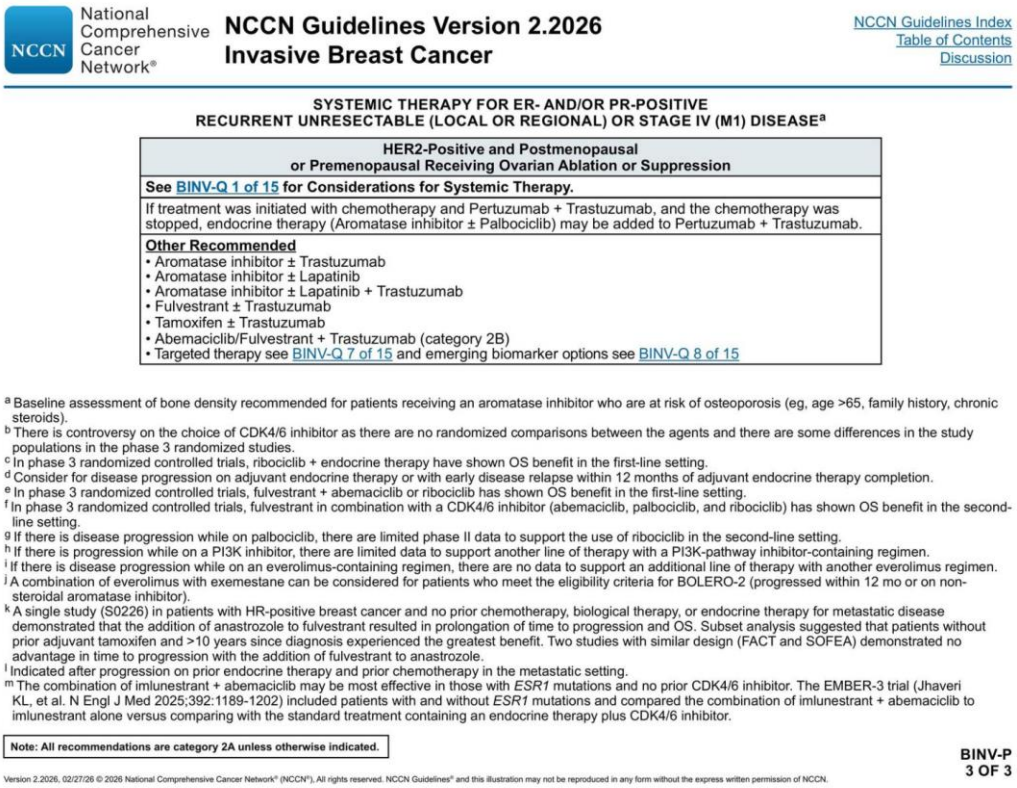

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SYSTEMIC THERAPY FOR ER- AND/OR PR-POSITIVE RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[a]

HER2-Positive and Postmenopausal or Premenopausal Receiving Ovarian Ablation or Suppression
See BINV-Q 1 of 15 for Considerations for Systemic Therapy.
If treatment was initiated with chemotherapy and Pertuzumab + Trastuzumab, and the chemotherapy was stopped, endocrine therapy (Aromatase inhibitor ± Palbociclib) may be added to Pertuzumab + Trastuzumab.
Other Recommended • Aromatase inhibitor ± Trastuzumab • Aromatase inhibitor ± Lapatinib • Aromatase inhibitor ± Lapatinib + Trastuzumab • Fulvestrant ± Trastuzumab • Tamoxifen ± Trastuzumab • Abemaciclib/Fulvestrant + Trastuzumab (category 2B) • Targeted therapy see BINV-Q 7 of 15 and emerging biomarker options see BINV-Q 8 of 15

[a] Baseline assessment of bone density recommended for patients receiving an aromatase inhibitor who are at risk of osteoporosis (eg, age >65, family history, chronic steroids).
[b] There is controversy on the choice of CDK4/6 inhibitor as there are no randomized comparisons between the agents and there are some differences in the study populations in the phase 3 randomized studies.
[c] In phase 3 randomized controlled trials, ribociclib + endocrine therapy have shown OS benefit in the first-line setting.
[d] Consider for disease progression on adjuvant endocrine therapy or with early disease relapse within 12 months of adjuvant endocrine therapy completion.
[e] In phase 3 randomized controlled trials, fulvestrant + abemaciclib or ribociclib has shown OS benefit in the first-line setting.
[f] In phase 3 randomized controlled trials, fulvestrant in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, and ribociclib) has shown OS benefit in the second-line setting.
[g] If there is disease progression while on palbociclib, there are limited phase II data to support the use of ribociclib in the second-line setting.
[h] If there is progression while on a PI3K inhibitor, there are limited data to support another line of therapy with a PI3K-pathway inhibitor-containing regimen.
[i] If there is disease progression while on an everolimus-containing regimen, there are no data to support an additional line of therapy with another everolimus regimen.
[j] A combination of everolimus with exemestane can be considered for patients who meet the eligibility criteria for BOLERO-2 (progressed within 12 mo or on non-steroidal aromatase inhibitor).
[k] A single study (S0226) in patients with HR-positive breast cancer and no prior chemotherapy, biological therapy, or endocrine therapy for metastatic disease demonstrated that the addition of anastrozole to fulvestrant resulted in prolongation of time to progression and OS. Subset analysis suggested that patients without prior adjuvant tamoxifen and >10 years since diagnosis experienced the greatest benefit. Two studies with similar design (FACT and SOFEA) demonstrated no advantage in time to progression with the addition of fulvestrant to anastrozole.
[l] Indicated after progression on prior endocrine therapy and prior chemotherapy in the metastatic setting.
[m] The combination of imlunestrant + abemaciclib may be most effective in those with *ESR1* mutations and no prior CDK4/6 inhibitor. The EMBER-3 trial (Jhaveri KL, et al. N Engl J Med 2025;392:1189-1202) included patients with and without *ESR1* mutations and compared the combination of imlunestrant + abemaciclib to imlunestrant alone versus comparing with the standard treatment containing an endocrine therapy plus CDK4/6 inhibitor.

Note: All recommendations are category 2A unless otherwise indicated.

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IV CONCLUSÕES:

- ✓ A combinação de Pertuzumabe + Trastuzumabe, tem cobertura da ANS para câncer de mama, geralmente em associação com outra quimioterapia (por exemplo docetaxel), conforme prescrição médica. O anastrozol não é quimioterapia e sim hormonioterapia não tendo cobertura pela ANS
- ✓ Na literatura existe indicação da combinação de Pertuzumabe + Trastuzumabe + Anastrozol em alguns casos
- ✓ A solicitação da medicação é de 14/02/2025 e 23/12/2024 e deve ser revista uma vez que se trata de doença progressiva
- ✓ Idealmente deve ser realizada perícia médica para definir o benefício da medicação solicitada em 14/02/2025 e 23/12/2024 para o quadro atual da paciente; apesar de existir indicação na literatura essa iniciação pode ter ser perdido com tempo não trazendo mais benefício para paciente

V– REFERÊNCIAS:

Pertuzumab, Trastuzumab, and an Aromatase Inhibitor for HER2-Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer: PERTAIN Final Analysis.
Clinical Cancer Research : An Official Journal of the American Association for Cancer Research. 2023. Arpino G, de la Haba Rodríguez J, Ferrero JM, et al.

2.

Breast Cancer.

National Comprehensive Cancer Network. Updated 2026-02-27.

3.

Efficacy of Endocrine Therapy Plus Trastuzumab and Pertuzumab vs De-escalated Chemotherapy in Patients with Hormone Receptor–Positive/-ERBB2-Positive Early Breast Cancer: The Neoadjuvant WSG-TP-II Randomized Clinical Trial.

JAMA Oncology. 2023. Gluz O, Nitz UA, Christgen M, et al.

4.

First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without Pertuzumab, in Human Epidermal Growth Factor Receptor 2-Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial.

Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2018. Rimawi M, Ferrero JM, de la Haba-Rodriguez J, et al.

VI –DATA:31/03/2026

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