Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of breast cancer

***Update v1.2**: Table 2 was updated from the original publication to include the GARNET trial data that led to the tissue-agnostic dostarlimab approval. For the full guideline text and other updates included in v1.2, please see https://doi.org/10.1136/jitc-2021-002597.*

Table 2: Trials of ICIs for recurrent/metastatic breast cancer and tissue-agnostic indications

Trial name	Phase	Setting	Control and immunotherapy arms	Key outcome measures for FDA approval
Trials leading to FDA approvals				
IMpassion130	III	Previously untreated TNBC	Control (n = 451): Placebo + nab-paclitaxel Immunotherapy (n = 451): Atezolizumab + nab-paclitaxel	**PD-L1 IC+** PFS 7.5 vs 5.0 months HR 0.62 (95% CI 0.49 to 0.78; p < 0.001) **ITT** PFS 7.2 vs 5.5 months HR 0.80 (95% CI 0.69 to 0.92; p = 0.002)
KEYNOTE-355	III	Previously untreated TNBC	Control (n = 281): Placebo + investigator's choice: nab-paclitaxel, paclitaxel, or gemcitabine and carboplatin Immunotherapy (n = 566): Pembrolizumab + investigator's choice: nab-paclitaxel, paclitaxel, or gemcitabine and carboplatin	**CPS ≥ 10** PFS 9.7 vs 5.6 months HR 0.65 (95% CI 0.49 to 0.86; p = 0.0012) **CPS ≥ 1** PFS 7.6 vs 5.6 months HR 0.74 (95% CI 0.61 to 0.90; p = 0.0014)

Hypothesis-generating trials				
KEYNOTE-119	III	TNBC that has progressed on prior therapy	Control (n = 310): Investigator's choice: capecitabine, eribulin, gemcitabine, or vinorelbine Immunotherapy (n = 312): Pembrolizumab	**CPS ≥ 10** OS 12.7 vs 11.6 months HR 0.78 (95% CI 0.57 to 1.06; p = 0.0574) **CPS ≥ 1** OS 10.7 vs 10.2 months HR 0.86 (95% CI 0.69 to 1.06; p = 0.0728) **ITT** OS 9.9 vs 10.8 months HR 0.97 (95% CI 0.82 to 1.15)
IMpassion131	III	Previously untreated TNBC	Control (n = 220): Placebo + paclitaxel Immunotherapy (n = 431): Atezolizumab + paclitaxel	**PD-L1 IC+** PFS 6.0 vs 5.7 months HR 0.82 *(p* = 0.20) **ITT** OS 19.2 vs 22.8 months HR 1.11
KATE2	II	HER2+ breast cancer with prior trastuzumab and taxane therapy	Control (n = 69): Placebo + trastuzumab emtansine Immunotherapy (n = 133): Atezolizumab + trastuzumab emtansine	**ITT** Median PFS 8.2 vs 6.8 months HR = 0.82 (95% CI 0.55 to 1.23; p = 0.33)
Trials leading to tissue-agnostic approvals				
Pooled analysis: KEYNOTE-016 KEYNOTE-164 KEYNOTE-012	Multi-cohort, single-arm	MSI-H or dMMR tumors that have progressed	Immunotherapy (n =149; 5 patients with breast cancer): Pembrolizumab	ORR 39.6% (95% CI 31.7 to 47.9) CR rate 7%

KEYNOTE-028 KEYNOTE-158		on prior therapy		DOR 1.6+ to 22.7+ months (78% lasting ≥ 6 months)
KEYNOTE-158	Multi-cohort, single-arm	TMB-H tumors (≥ 10 mut/Mb) that have progressed on prior therapy	Immunotherapy (n = 102; 0 patients with breast cancer): Pembrolizumab	ORR 29% (95% CI 21 to 39) CR rate 4% Median DOR not reached (57% lasting ≥ 12 months; 50% lasting ≥ 24 months)
GARNET	Multi-cohort, single-arm	Recurrent or advanced **dMMR** solid tumors that have progressed on prior therapy	Immunotherapy (n=209): Dostarlimab	ORR 41.6% (95% CI 34.9% to 48.6%) CR rate 9.1% Median DOR 34.7 months (range 2.6 to 35.8+) (95.4% lasting ≥6 months)

***The accelerated approval for atezolizumab in combination with nab-paclitaxel was voluntarily withdrawn in 2021.*

Abbreviations used: CI, confidence interval; CPS, combined positive score; CR, complete response; dMMR, mismatch-repair deficient; DOR, duration of response; HR, hazard ratio; IC, immune cell; ITT, intent-to-treat; MSI-H, microsatellite instability high; ORR, overall response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; R/M, recurrent/metastatic; TMB-H, high tumor mutation burden.

Source: Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of breast cancer v1.2. SITC Breast Cancer CPG informational website – Updates since publication