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2018 at a glance: Recently approved therapies in oncology

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Advances in genomics and technology perpetually change and improve therapies in oncology. Enhanced comprehension of cellular signaling, division, and replication has created a platform to selectively restrict neoplastic growth while preserving the integrity of benign cells.

This article reviews therapies that were newly approved in 2018, as well as those previously approved whose indications were expanded this past year. The list highlights the most clinically important approvals, as well as adverse events that are unique or especially severe.

Apalutamide (Erleada)

Class: Androgen receptor inhibitor.
Disease: Nonmetastatic castration-resistant prostate cancer.
Dose: 240 mg orally, once daily.
Adverse Events (AEs): Hyperkalemia and increased risks of seizures, falls, and fractures.
Phase 3 SPARTAN trial (NCT01946204): 40.5-month metastasis-free survival rate, compared with 16.2 months in the placebo group.

Cemiplimab (Libtayo)

Class: Antibody against programmed cell death protein-1 (PD-1).
Disease: Metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC that is ineligible for curative surgery/radiation.
Dose: 350 mg intravenous infusion every 3 weeks.
AEs: Pneumonitis, autoimmune myocarditis, hepatitis, and aseptic meningitis.
1423 and 1540 trials (NCT02383212 and NCT02760498): 47.2% of patients who received cemiplimab had complete disappearance of the tumor or a decrease in tumor size.

Dacomitinib (Vizimpro)

Class: Second-generation tyrosine kinase inhibitor.
Disease: Metastatic non–small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutation.
Dose: 45 mg orally once daily.
AEs: Dermatotoxicity and diarrhea.
ARCHER1050 trial (NCT01774721): Patients who received dacomitinib demonstrated an improved overall survival, with a median of 34.1 months, compared with 26.8 months with gefitinib.

Duvelisib (Copiktra)

Class: Dual inhibitor of phosphatidylinositol 3-kinase delta and gamma.
Disease: Relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, or relapsed or refractory follicular lymphoma after at least two prior systemic therapies.
Dose: 25 mg orally twice daily.

Expanded indications for previously approved drugs

Drug name	Previous indication	New indication	Landmark study
Olaparib (Lynparza)	• Maintenance recurrent ovarian cancer • Advanced germline BRCA mutated ovarian cancer	• First-line maintenance for BRCA-mutated advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer	SOLO-1 (NCT01844986)
Pembrolizumab (Keytruda)	• Unresectable or metastatic melanoma • Unresectable or metastatic solid tumors that are microsatellite instability–high or mismatch repair deficient • Metastatic NSCLC with high program death-ligand 1 expression • Recurrent or metastatic NSCLC • Classical Hodgkin lymphoma • Recurrent or metastatic cervical cancer	• Recurrent locally advanced or metastatic Merkel cell carcinoma • Hepatocellular carcinoma in patients who received sorafenib • First-line treatment in combination with chemotherapy for metastatic squamous NSCLC	KEYNOTE-017 (NCT02267603) KEYNOTE-224 (NCT02702414) KEYNOTE-407 (NCT02775435)
Nivolumab (Opdivo)	• Metastatic melanoma • Metastatic NSCLC • Renal cell carcinoma • Hodgkin lymphoma • Recurrent or metastatic head and neck squamous cell carcinoma • Locally advanced or metastatic urothelial carcinoma • Microsatellite instability–high or mismatch repair deficient metastatic colorectal cancer • Hepatocellular carcinoma	• Metastatic small-cell lung cancer with progression after platinum-based therapy and an additional therapy	CHECKMATE-032 (NCT01928394)
Brentuximab vedotin (Acetris) combined with chemotherapy	• Cutaneous anaplastic large cell lymphoma • CD30-expressing mycosis fungoides • Classical Hodgkin lymphoma at high risk of relapse or progression after auto-HSCT consolidation • Classical Hodgkin lymphoma after failure of auto-HSCT or after failure of at least two prior multiagent therapies	• Previously untreated systemic anaplastic large-cell lymphoma or other CD30-expressing peripheral T-cell lymphomas	ECHELON-2 (NCT01777152)
Dabrafenib (Tafinlar) combined with Trametinib (Mekinist)	• Metastatic NSCLC with BRAF 600E mutation	• Unresectable or metastatic BRAF V600E mutation–positive anaplastic thyroid cancer • Melanoma with BRAF V600E or V600K mutations	BRF117019 (NCT02034110) COMBI-AD (NCT01682083)
Blinatumomab (Blincyto)	• Relapsed or refractory Philadelphia chromosome–negative B-cell precursor acute lymphoblastic leukemia • Relapsed or refractory Philadelphia chromosome–positive B-cell precursor acute lymphoblastic leukemia	• B-cell precursor acute lymphoblastic leukemia who are in remission but still have minimal residual disease	BLAST (NCT01207388)

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Note: NSCLC = non–small cell lung cancer, HSCT = hematopoietic stem cell transplantation, BRAF = v-raf murine sarcoma viral oncogene homolog B1.
Source: Dr. Bryer, Dr. Mintzer, and Dr. Henry

AEs: Infection, diarrhea or colitis, and pneumonia.
Phase 3 DUO trial (NCT02004522): Progression-free survival in the duvelisib arm was 7.3 months longer than that in the ofatumumab arm. The overall response rate for patients receiving duvelisib was 78%, compared with 39% for those receiving ofatumumab.

Gilteritinib (Xospata)

Class: Inhibits the FLT3 internal tandem duplication (ITD) and FLT3 tyrosine kinase domain (TKD).
Disease: Relapsed or refractory acute myeloid leukemia (AML) with an FLT3 mutation.
Dose: 120 mg orally daily.
ADMIRAL trial (NCT02421939): 21% of the patients who received gilteritinib exhibited complete remission or complete remission with partial hematologic recovery.

Glasdegib (Daurismo)

Class: Hedgehog pathway inhibitor.
Disease: Adults over age 75 years with newly diagnosed AML and other medical comorbidities that preclude them from intensive chemotherapy.
Dose: The recommended dose is 100 mg orally continuously in 28-day cycles.
AE: QT prolongation and embryo-fetal toxicity
Phase 2 BRIGHT 1003 trial (NCT01546038): 3.9-month overall survival advantage for glasdegib plus cytarabine, compared with cytarabine alone. Overall, 15% of the glasdegib plus low dose cytarabine arm achieved complete remission, compared with the 1% complete remission rate in patients who received cytarabine alone.

Iobenguane I 131 (Azedra)

Class: Radiopharmaceutical agent; induces cell death within the noradrenaline transporter.
Disease: Iobenguane scan–positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma
Dose: Initial intravenous dosimetric dose, followed by two therapeutic doses.
AE: Pancytopenia and elevated international normalized ratio (INR).
IB12B trial (NCT00874614): One-quarter of patients receiving this therapy had at least a 50% reduction in the dose and number of antihypertensives for at least 6 months; almost all patients had a tumor response.

Ivosidenib (Tibsovo)

Class: Small-molecule inhibitor of mutant isocitrate dehydrogenase (IDH1).
Disease: Refractory AML and an IDH1 mutation
Dose: 500 mg orally daily.
AG120-C-001 trial (NCT02074839): Overall response rate of 41.6% in patients who received ivosidenib, with a 30.4% rate of complete remission or complete remission with partial hematologic recovery.

2018 biosimilars

Name	Biosimilar to:	Indication
Adalimumab-adaz (Hyrimoz)	Adalimumab	• Rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis, plaque psoriasis
Epoetin alfa-epbx (Retacrit)	Epoetin alfa	• Anemia related to chronic kidney disease, zidovudine with HIV infection, myelosuppressive chemotherapy • Reduction of allogenic red blood cell transfusions in elective and noncardiac/nonvascular surgery
Filgrastim-aafi (Nivestym)	Filgrastim	• Decrease incidence of infection in patients receiving myelosuppressive chemotherapy • Reduce the time to neutrophil recovery and duration of fever in patients with acute myeloid leukemia • Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
Pegfilgrastim-jmdb (Fulphila)	Pegfilgrastim	• Decrease the incidence of infection in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of febrile neutropenia
Pegfilgrastim-cbqv (Udenyca)	Pegfilgrastim	• *Same indications as pegfilgrastim-jmdb*
Rituximab-abbs (Trumixa)	Rituximab	• CD20-positive B-cell non-Hodgkin lymphoma
Trastuzumab-pkrb (Herzuma)	Trastuzumab	• HER2-overexpressing breast cancer

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Source: Dr. Bryer, Dr. Mintzer, and Dr. Henry

Larotrectinib (Vitrakvi)

Class: Oral tyrosine kinase inhibitor.
Disease: Advanced solid tumors harboring a neurotrophic tyrosine receptor kinase (NTRK) gene fusion.
Dose: 100 mg orally twice daily.
LOXO-TRK-14001, SCOUT, and NAVIGATE trials (NCT02122913, NCT02637687, and NCT02576431): Patients who received larotrectinib had durable responses regardless of patient age, tumor type, and fusion status.

Lutetium Lu 177 dotatate (Lutathera)

Class: Radiolabeled somatostatin analogue.
Disease: Somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs).
Dose: Intravenous infusion 7.4 GBq (200 mCi) every 8 weeks for a total of four doses.
NETTER-1 trial (NCT01578239): 65% of adults who received lutetium Lu 177 showed improved progression-free survival at 20 months, compared with just 10.8% in the control group.

Mogamulizumab (Poteligeo)

Class: Monoclonal antibody that binds to a protein (CC chemokine receptor type 4).
Disease: Relapsed or refractory mycosis fungoides or Sézary syndrome.
Dose: Intravenous infusion 1 mg/kg.
AE: Dermatologic toxicity.
MAVORIC trial (NCT01728805): Patients who received mogamulizumab had improved progression-free survival (median 7.7 months), compared with those taking vorinostat (median 3.1 months).

Moxetumomab pasudotox-tdfk (Lumoxiti)

Class: CD22-directed cytotoxin fused with a fragment of Pseudomonas exotoxin A.
Disease: Relapsed or refractory hairy cell leukemia previously treated with at least two prior systemic therapies, including a purine nucleoside analogue.
Dose: Intravenously as 0.04 mg/kg.
AE: Hemolytic uremic syndrome.
1053 trial (NCT01829711): 30% of the patients who received moxetumomab pasudotox-tdfk had a durable complete response confirmed by maintenance hematologic remission.

Talazoparib (Talzenna)

Class: Poly (ADP-ribose) polymerase (PARP) inhibitor.
Disease: gBRCAm HER2-negative locally advanced or metastatic breast cancer.
Dose: 1 mg orally per day.
EMBRACA trial (NCT01945775): Patients who received talazoparib demonstrated significantly longer progression-free survival, with a median of 8.6 months versis 5.6 months in the control arm.

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