

Advanced & Immuno- Therapies

by Helena Pasieka, MD

Generic Name	Brand Name	Route	Category	Mechanism of Action	Indication	Side Effects	Other
Imatinib (1st gen) Dasatinib/ Nilotinib (2nd gen)	Gleevec Sprycel, Tasigna	PO	Category D	Inhibit tyrosine kinases <i>bcr/abl</i> (<i>chrom 9:22 translocation</i>).	CML. Also used in DFSP, AIDS-related KS, KIT-mutated melanoma, & subgroup of patients with hypereosinophilic syndrome.	Superficial edema periorbital edema (imatinib); pleural effusions (dasatinib). Localized, patchy, or diffuse hypopigmentation, caused by inhibition of <i>c-kit</i> , usu. reversible.	
Gefitinib, Erlotinib, Cetuximab, Panitumumab	Iressa, Tarceva, Erbitux, Vectibix	PO IV	Category C	EGFR inhibitors	Non-small cell lung cancer, pancreatic cancer.	PRIDE syndrome = <i>Papulopustular rash and/or Paronychia, Regulatory change in hair (including eyelash trichomegaly), Itching, Dryness</i> caused by EGFRi.	Severity of rash has been directly correlated with an increase in survival (in some studies). Eruption is seen with both monoclonal Ab and TK inhibitor versions of the drug.
Vismodegib	Erivedge	PO	Category D	PTCH analog (binds and inhibits the Smoothed R), leading to hedgehog signaling pathway inhibition and decreased tumor cell proliferation.	Metastatic BCC, locally aggressive BCC w/recur after surgery; BCC not candidate for XRT or surgery. Off label for use in basal cell nevus syndrome.	Muscle spasms (68%) & reversible alopecia (63%), dysgeusia (51%)	Black box warning: Teratogenicity. Women to contraindicated for 7 months. 3 months condom with spermicide for men. No blood donation by either sex for 7 months.
Bortezomib	Velcade	IV/SQ	Category D	Proteasome inhibitor, may prevent degradation of pro-apoptotic factors, permitting activation of programmed cell death in neoplastic cells; dependent upon suppression of pro-apoptotic pathways.	Multiple myeloma, NHL, Mantle cell Lymphoma.	GI distress, weakness & peripheral neuropathy, myelosuppression . Sweet syndrome.	
Sorafenib	Nexavar	PO	Category D	Multikinase inhibitors, which target tumor cell angiogenesis and proliferation via CEGFR, PDGFR, and others.	Hepatocellular carcinoma, renal cell carcinoma, differentiated thyroid carcinoma; also, unresectable or metastatic melanoma.	Specific hand-foot reaction with painful, localized patches on friction/trauma prone surfaces (such as heel, lateral soles, web spaces). Usually hyperkeratotic with superficial blistering; Stomatitis; genital involvement Alopecia; brittle, curly, depigmented hair; facial rash that looks like sebDerm; subungual splinter hemorrhages; yellow skin pigmentation. Development of new SCCs, benign dyskeratomas , generalized KP-like eruption.	
Vemurafenib, Dabrafenib	Zelboraf, Tafinlar	PO	Category D	Selective inhibitors of the BRAF V600E oncoprotein. Present in >80% of cutaneous melanoma.	Unresectable or metastatic melanoma (V600E mutation only).	Papulopustular rash on face, torso, and arms. Development of SCC and KA (treat by excision, not dose modification), photosensitivity , KP-or SebDerm like eruption, panniculitis, alopecia.	Risk of QT prolongation , therefore contraindicated with Ranolazine, Dronedrone, Phenothiazines, Pimozide. Frequent monitoring with visits every 4-6 weeks at baseline, then every month for first six months of therapy, then every 8 weeks.
Trametinib	Mekinist	PO	Category D	MEK inhibitor.	Unresectable or metastatic melanoma with BRAF V600E or V600K gene mutation.	MEK inhibitors have SE similar to EGFR inhibitors .	Combination of MEK inhibition with BRAF inhibition shows reduction in BRAF inhibitor resistance and decreased incidence of SCC SE.
Rapamycin, Everolimus, Temsirolimus	Rapamune, Afinitor, Torisel	PO	Category C	mTOR inhibitor: (on the PI3K - AKT - mTOR pathway)	Prophylaxis of organ rejection. Also used in blue rubber bleb nevus syndrome, angiofibromas, Kaposi's sarcoma, lymphangioma circumscriptum, CLOVES syndrome.	Stomatitis , morbilliform inflammatory eruption, nail toxicity (paronychia, pyogenic granuloma).	



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Ipilimumab	Yervoy	IV	Category C	CTLA-4 inhibitor: Fully humanized monoclonal antibody (IgG ₁) that blocks cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) to promote an antitumor T-cell response (aka: CD152 antibody)	Unresectable or metastatic melanoma.	Autoimmune dermatopathies & immune-related diarrhea/colitis.	Appearance of vittiligo-like melanoma-associated hypopigmentation (MAH) portends favorable response to therapy.
Nivolumab, Pembrolizumab	Opdivo Keytruda	IV	Category D	PD-1 Inhibitor: Binds to the PD-1 receptor on T-cells, blocking PD-1 pathway-mediated anti-tumor immune response inhibition (monoclonal Ab)	Unresectable or metastatic melanoma.	Pruritus (50%), rashes of multiple morphologies, and vitiligo.	There is evidence in melanoma for synergy between CTLA-4 and PD-1/PD-L1, which is consistent with the distinct and complementary roles of the two molecules in the regulation of T cell responses.
Alemtuzumab	Campath	IV/SQ	Category C	Humanized monoclonal antibody against the CD52 surface Ag on immune cells, including T/B cells.	B-cell chronic lymphocytic leukemia. Also cutaneous T-cell lymphoma (CTCL) with peripheral blood disease.	Lymphopenia, urticaria, various rashes, and erythema.	Black box: Cytopenias, infusion reactions, and infections
Romidepsin Vorinostat	Istodax Zolinza	IV PO	Category D	Histone deacetylase inhibitors (HDAC inhibitors)	Treatment of cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy.	GI sx, fatigue, heme abnmlity ("penias"), infectious complications. T wave flattening in 71% of patients.	
Brentuxmab-vedotin	Adcetris	IV	Category D	Phosphoinositide 3-kinase inhibitors.	CD30+ mycosis fungoides and Sézary syndrome, anaplastic large cell lymphoma.	Neutropenia, peripheral sensory neuropathy, fatigue, and nausea.	Black box: JC virus infection resulting in PML.
Denileukin diftitox	Ontak	IV	Category C	Binds to IL-2-alfa receptor or CD25 and introduces the diphtheria toxin into cells, killing the cells.	Persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor.	Acute infusion-related events, myalgia, elevated LFTs, and vascular leak syndrome	Black box: (1) Serious and fatal infusion reactions. (2) Capillary leak syndrome resulting in death. (3) Loss of visual acuity and color vision.
Lenalidomide	Revlimid	PO	Category X	Thalidomide analog , increases TH1-cytokine production and enhances T and NK cell-mediated killing.	FDA: myelodysplastic syndrome, relapsed/refractory multiple myeloma, mantle cell lymphoma. Also in CTCL and Sézary.	Temporary flares of skin disease & circulating Sézary cells, cytopenias , and fatigue/malaise.	
Aprepitant Fosaprepitant	Emend	PO IV	Category B	Selectively antagonizes human substance P/ neurokinin 1 receptors.	Prevention of n/v with highly emetogenic chemotherapy. Also used in refractory pruritus in CTCL, Sézary, trialed in brachioradial pruritus, other pruritis.	Fatigue, diarrhea.	

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Tofacitinib	Xeljanz	PO	Category C	Janus kinase (JAK) inhibitor	Rheumatoid arthritis. Also, alopecia areata, graft vs. host disease.	Upper respiratory tract infections, headache, diarrhea, and nasopharyngitis.	Black box warnings: (1) Death from serious infections, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections; (2) Monitor all patients for active TB during treatment, even if the initial TB test is negative; (3) Lymphoma and other malignancies have been observed. EBV-associated post-txplnt lymphoproliferative d/o at an increased rate in renal txplnt pts with concomitant immunosuppressive medications.
Anakinra	Kineret	SQ	Category B	Recombinant, non-glycosylated version of human IL-1 receptor antagonist -> competitive inhibitor of IL-1.	Rheumatoid arthritis. Also, Schnitzler's syndrome, cryopyrin-ass'd periodic fever syndromes (MW, Familial cold autoinflammatory syndrome, NOMID [aka: infantile neurologic cutaneous and articular syndrome= CINCA], HIDS).	Flu-like sx, infxn, neutropenia, thrombocytopenia.	Do not give with TNF-alpha inhibitors or live vaccines. Contraindicated in renal failure/impairment or hypersensitivity to the drug.