cutis° **FAST FACTS** for BOARD REVIEW

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Medications for Advanced Melanoma

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Generic Name	Brand Name (Manufacturer)	Mechanism of Action	Method of Administration	Cutaneous Side Effects	Drug Efficacy From Phase 3 Clinical Trials	Notes
BRAF Inhibitors Dabrafenib	Tafinlar (GlaxoSmithKline)	Blocks BRAF mutations in the Ras/ ERK pathway preventing cell proliferation	Oral pill	Eruptive SCC, keratosis pilaris, seborrheic dermatitis—like eruptions	5 mo median PFS vs 2.7 mo on dacarbazine	Indicated as monotherapy for patients with unresectable or metastatic melanoma with BRAF V600E mutations; used in combination with trametinib for BRAF V600E or V600K mutations; not indicated for wild-type BRAF melanoma
Vemurafenib	Zelboraf (Genentech USA, Inc)	Blocks BRAF mutations in the Ras/ERK pathway preventing cell proliferation	Oral pill	Eruptive SCC, keratosis pila- ris, seborrheic dermatitis-like eruptions	4 mo increase in median PFS vs dacar- bazine; 3 mo improvement in median OS compared to dacarbazine	Indicated for unresectable or metastatic mela- noma with <i>BRAF</i> V600E mutation; not indicated for wild-type <i>BRAF</i> melanoma
MEK Inhibitors Trametinib	Mekinist	Blocks <i>BRAF</i>	Oral pill	Morbilliform	3 mo	Indicated as
	(GlaxoSmithKline)	mutations in the Ras/ERK pathway preventing cell proliferation		eruption, acne/rosacea, dry skin	improvement in median OS compared to traditional chemotherapy	monotherapy and in com- bination with dabrafenib in patients with unresectable or metastatic mela- noma with <i>BRAF</i> V600E or V600K mutations
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(continued)					Drug Efficacy	
Generic Name	Brand Name (Manufacturer)	Mechanism of Action	Method of Administration	Cutaneous Side Effects	From Phase 3 Clinical Trials	Notes
MEK Inhibitors (C	ontinued)					
Cobimetinib	N/A	Blocks BRAF mutations in the Ras/ERK pathway preventing cell proliferation	Oral pill	SCC, photosensitiv- ity, morbilliform eruption	3 mo improve- ment in median OS when combined with vemurafenib vs vemurafenib alone	Not yet FDA approved; has shown improved survival when combined with vemurafenib for <i>BRAF</i> V600 mutation
Antibodies						
Pembrolizumab	Keytruda (Merck & Co, Inc)	Human IgG4 monoclonal antibody to PD-1, causes T-cell activation	IV infusion	Pruritus, morbilliform eruption	Overall response rate was 24%, median OS was 18 mo	Indicated for unresectable or metastatic melanoma and disease progression following ipilimumab and a BRAF inhibitor if <i>BRAF</i> V600 mutation positive
Nivolumab	Opdivo (Bristol- Myers Squibb Company)	Human IgG4 monoclonal antibody to PD-1, causes T-cell activation	IV infusion	Morbilliform eruption	Median PFS was 11.5 mo with nivolumab + ipilimumab, 2.9 mo with ipilimumab alone, and 6.9 mo with nivolumab alone	Indicated for unresectable or malignant melanoma and disease progression following ipilimumab and a BRAF inhibitor if <i>BRAF</i> V600 mutation positive
Ipilimumab	Yervoy (Bristol-Myers Squibb Company)	Monoclonal antibody to CTLA-4, prevents T-cell inactivation	IV infusion	Morbilliform eruption, TEN	Average OS for ipilimumab + gp100 was 10.1 mo compared to 6.4 mo with gp100 alone	Indicated for unresectable or metastatic melanoma, can result in severe and fatal immunemediated reactions involving any organ system (most common are enterocolitis, hepatitis, neuropathy, and endocrinopathy)

(continued)	Brand Name	Mechanism	Method of	Cutaneous	Drug Efficacy From Phase 3 Clinical	
Generic Name	(Manufacturer)	of Action	Administration	Side Effects	Trials	Notes
Alfa Interferons						
Recombinant interferon alfa-2b	Intron A (Merck & Co, Inc)	Direct antipro- liferative effect, enhancement of natural killer cell activity, upregulation of tumor antigens and HLA class I and II antigens	IV infusion followed by SQ injection	Raynaud phenomenon, acute hypersensitivity reaction, worsening of sarcoidosis and psoriasis	3 mo PFS and similar efficacy to monochemo- therapy	Adjuvant to surgi- cal treatment in patients with high risk for systemic recurrence of malignant melanoma
Peginterferon alfa-2b	Sylatron (Merck & Co, Inc)	Direct antipro- liferative effect, enhancement of natural killer cell activity, upregulation of tumor antigens and HLA class I and II antigens	SQ injection	Urticaria, angioedema	Increase recurrence- free survival time by 8 mo compared to observation, no increase in OS	Indicated for adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy
IL-2 Cytokine						
Aldesleukin	Proleukin (Prometheus Laboratories, Inc)	IL-2 cytokine promotes T-cell activation	IV infusion	Morbilliform eruption, vitiligo	Overall objective response rate was 16%	
Other						
Dacarbazine	DTIC-Dome (Bayer Pharmaceuticals Corporation)	Purine analog that inhibits DNA synthe- sis, acts as an alkylating agent, interacts with sulfhydryl groups	IV infusion	Urticaria, angioedema	Mean PFS 2.3 mo	Not particularly efficacious for melanoma, response seen in <20% of patients

Abbreviations: ERK, extracellular signal-regulated kinase; SCC, squamous cell carcinoma; PFS, progression-free survival; OS, overall survival; MEK, mitogen-activated protein kinase; N/A, not available; FDA, US Food and Drug Administration; PD-1, programmed cell death protein 1; IV, intravenous; CTLA-4, cytotoxic T-lymphocyte-associated antigen 4; TEN, toxic epidermal necrolysis; SQ, subcutaneous.

Practice Questions

1. Which of the following medications is considered an MEK inhibitor?

- a. aldesleukin
- b. dacarbazine
- c. ipilimumab
- d. recombinant interferon alfa-2b
- e. trametinib

2. Which of the following medications has been shown to be associated with toxic epidermal necrolysis?

- a. aldesleukin
- b. dacarbazine
- c. ipilimumab
- d. recombinant interferon alfa-2b
- e. trametinib

3. What medication can be administered as a subcutaneous injection?

- a. aldesleukin
- b. dacarbazine
- c. ipilimumab
- d. recombinant interferon alfa-2b
- e. trametinib

4. Which of the following medications is a monoclonal antibody to cytotoxic T-lymphocyte-associated antigen 4?

- a. aldesleukin
- b. dacarbazine
- c. ipilimumab
- d. recombinant interferon alfa-2b
- e. trametinib

5. Which of the following medications is an IL-2 cytokine?

- a. aldesleukin
- b. dacarbazine
- c. ipilimumab
- d. recombinant interferon alfa-2b
- e. trametinib

Fact sheets and practice questions will be posted monthly. Answers are posted separately on www.cutis.com.