Managed Healthcare ExecutiveAMCP

Highly specific indications dominate cancer drug pipeline

October 18, 2017
By Bryant Furlow

Cancer drug development is increasingly targeted at very specific patient subpopulations, with a focus on targeting specific tumor gene mutations and molecular pathways, according to a presenter at the Academy of Managed Care Pharmacy (AMCP) 2017 Nexus.

Antineoplastic agents represent a growing proportion of specialty drug spending, said Edward Li, PharmD, MPH, BCOP, a professor at the University of New England College of Pharmacy in Portland, Maine, during his October 17 session.

Li reviewed the evidence base for three key cancer therapies likely to be FDA approved in the coming year that could change treatment guidelines and improve outcomes, and the overall implications for cancer expenditures.

"Expenditures for oral oncolytics increased to $6 billion in 2012 from 1 billion in 2003," Li said. "The percent dispensed through specialty pharmacy increased to 61% from 26%."

Potential 2018 approvals include three key oral agents, Li reported:

- The CDK4/6 inhibitor verzenio (abemaciclib, Eli Lilly)
- The second-generation Bruton's tyrosine kinase (BTK) inhibitor acalabrutinib (Acerta)
- The tropomyosin kinase receptor inhibitor larotrectinib (Loxo Oncology).

"Since all three agents are designated as breakthrough therapies, the data demonstrating their clinical utility is not yet mature," he cautioned. "The overall potential impact of these agents on overall oncology drug spending is expected to be low to moderate."

Abemaciclib is more selective for CDK4 than CDK6 or 9, with absorption across the blood-brain barrier, Li noted. It can be dosed continuously as a monotherapy or with fulvestrant hormone therapy despite higher rates of diarrhea. It involves less bone-marrow suppression than other CDK inhibitors. Approved by the FDA in September 2017 for use with fulvestrant for patients with endocrine-therapy-refractory disease, abemaciclib was developed for hormone receptor-positive, HER2-negative advanced breast cancer for postmenopausal patients with prior endocrine therapy.

"We have had two seminal studies," Li said. The studies enrolled women in "ultra-last-stage settings" with endocrine-therapy-refractory disease, he said.

Overall survival data is not yet available but abemaciclib is associated with prolonged progression-free survival, Li said.

Abemaciclib with fulvestrant will compete with palbociclib as a second-line therapy after endocrine treatment fails, Li said.

Abemaciclib will serve a niche population of patients with cancer: those with tumors refractory to prior endocrine therapy and one or two chemotherapies, including a taxane, and who have had no prior exposure to CDK4/6 inhibitors, Li said.

Abemaciclib will have a moderate impact on biologics spending, Li predicted. "We will see low-moderate use as a single agent, depending on how many patients are CDK4/6 naïve," he said. "It will replace palbociclib to some degree."

Next: Acalabrutinib

Acalabrutinib

Acalabrutinib for previously-treated mantle cell lymphoma (MCL) and relapsed chronic lymphocytic leukemia (CLL) is an irreversible BTK inhibitor that is "designed to be more potent and selective than ibrutinib," Li said. Acalabrutinib's selectivity minimizes off-target toxicities, like hemorrhage, skin rash, and diarrhea, he noted. Unlike ibrutinib, it does not target tumors' EGFR, ITK, or TEC molecular pathways, and produces fewer off-target effects in healthy T-cells.

If approved by the FDA, acalabrutinib will compete with ibrutinib to treat refractory MCL and CLL/small cell lymphoma, with a potential niche as a combination therapy with the immunotherapy pembrolizumab for solid tumors.

"Acalabrutinib's relatively favorable toxicity profile may push ibrutinib out of MCL and CLL [treatment]," he said.

Larotrectinib

Nerve growth factors are important in several tumor types, including prostate, breast, pancreatic, thyroid, and melanoma skin cancers, and larotrectinib is a highly selective and potent inhibitor of three key nerve growth factor receptors, TRKA, TRKB, and TRKC, Li said. Several Phase 2 trials are underway among patients with tumors harboring NTRK fusion mutations and nervous system tumors.

That means that larotrectinib would be a very specific niche drug for "rare and heterogenous" tumors, if approved.

Li predicted that the FDA label would approve larotrectinib for the treatment of adult and pediatric refractory, advanced or metastatic cancers expressing NTRK1, NTRK2, or NTRK3 gene fusion mutations, when no alternative treatment options are available.

"The problem is, only 1% to 2% of tumors harbor these NTRK-fusion mutations—but there's a very specific unmet need for these patients," Li said. "If everything goes well, I think we're about a year out" from approval, he added.

Like acalabrutinib, larotrectinib is likely to have a modest impact on overall cancer specialty drug and biologic expenditures, Li predicted.

Li is a consultant for New Century Health and serves as an advisor for Mylan. He disclosed speaking honoraria from Pfizer and ApoBiologix.