Top 10 Cancer Treatment Highlights of 2018

A look back at some of the major news stories we covered this year.

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1. Pancancer Treatment Makes its Debut

In November, the Food and Drug Administration (FDA) approved Vitrakvi (larotrectinib), the first "site agnostic" or "pancancer" drug developed to treat cancer with specific genetic mutations anywhere in the body. Vitrakvi, from Loxo Oncology and Bayer, targets tropomyosin receptor kinase (TRK) proteins that are produced in cancer cells with a rare gene fusion. The latest data showed an overall response rate of 80 percent in a study of adults and children with more than a dozen types of cancer. In 2017, the checkpoint inhibitor Keytruda (pembrolizumab) received an additional indication for all tumors with genetic mutations known as high microsatellite instability or mismatch repair deficiency. Larotrectinib was the first medication originally developed and tested across cancer types, but it will not be the last: Loxo is working on a next-generation TRK inhibitor as well as LOXO-292, a drug that targets RET gene mutations. Blueprint's BLU-667 also targets RET gene mutations and fusions. Genentech's entrectinib targets both TRK fusions and ROS1 fusions, which play a role in lung cancer. Expect to see more of this new treatment paradigm in the future.

2. Immunotherapy in the News

Cancer immunotherapy made a splash in October when James Allison, PhD, of the University of Texas MD Anderson Cancer Center, and Tasuku Honjo, MD, PhD, of Kyoto University, won a Nobel Prize for discoveries that led to the development of checkpoint inhibitors. Initially developed to treat melanoma, research presented this year showed that PD-1/PD-L1 checkpoint blockers—which restore T-cell activity against cancer—hold promise for lung cancer (see next item), head and neck cancer and other solid tumors. Keytruda received an additional indication for liver cancer (joining Opdivo) and the FDA approved the new PD-1 checkpoint inhibitor Libtayo (cemiplimab-rwlc) for advanced cutaneous squamous cell carcinoma, a type of skin cancer. However, current immunotherapy does not work for all patients or all types of cancer and it remains difficult to predict who will benefit. Researchers are exploring new approaches to immune-based therapy in an effort to expand on its promise.

3. Checkpoint Inhibitors for Lung Cancer

There was so much news about immunotherapy for lung cancer that it warrants its own entry. The KEYNOTE-189 study showed that Keytruda plus Alimta (pemetrexed) and platinum chemotherapy delayed disease progression and improved overall survival for people with newly diagnosed metastatic non-small-cell lung cancer (NSCLC). KEYNOTE-042 showed that Keytruda without chemo may be enough for people with high PD-L1 levels in their tumors. The IMpower131, IMpower132 and IMpower150 trials found that first-line Tecentriq (atezolizumab) plus chemotherapy lowers the risk of disease progression or death in people with metastatic NSCLC. The PACIFIC trial showed that Imfinzi (durvalumab) led to slower disease progression and longer overall survival for people with Stage III NSCLC that cannot be surgically removed. Some people with lung cancer respond well to this type of treatment and remain in remission for years, but it still only works for a minority of patients.

4. CAR-T Therapy Offers Long-Term Benefit

Chimeric antigen receptor T-cell (CAR-T) therapy was the big breakthrough in 2017, with the approval of Novartis's Kymriah (tisagenlecleucel) for children with leukemia and Kite/Gilead's Yescarta (axicabtagene ciloleucel) for adults with lymphoma. Kymriah also got the nod for lymphoma this year. Longer-term data presented at this year's American Society of Hematology meeting showed that CAR-T therapy leads to sustained benefits for many patients. In the ELIANA trial of children and young adults with acute lymphoblastic leukemia, the estimated overall survival rate was 76 percent at 12 months and 66 percent at 24 months. The first child treated with Kymriah, Emily Whitehead, has now been cancer-free for more than six years. Success rates were not as high for adults with lymphoma in the ZUMA-1 and JULIET trials, but most of those who did respond had ongoing responses. Other experimental CAR-T therapies have shown good response rates for multiple myeloma and for chronic lymphocytic leukemia. But despite its promise, the high cost of CAR-T therapy and questions about how to pay for it have limited its use.

5. Good News for Metastatic Breast Cancer

Metastatic breast cancer continues to have a high mortality rate, but several new treatments offer hope. Immunotherapy generally does not work well against "cold" tumors like breast cancer. But in October, researchers reported that Tecentriq plus Abraxane (nab-paclitaxel) improved progression-free and overall survival for people with locally advanced or metastatic triple-negative breast cancer with PD-L1 positive tumors. Steven Rosenberg, MD, PhD, and his team at the National Cancer Institute showed that a novel immunotherapy approach using carefully selected tumor-infiltrating lymphocytes led to remission in a woman with previously unresponsive advanced breast cancer. This year also saw advances in targeted therapies. The FDA approved the PARP inhibitors Lynparza (olaparib) and Talzenna (talazoparib) for people with HER2-negative metastatic breast cancer with harmful BRCA mutations, the CDK4/6 inhibitor Kisqali (ribociclib) for premenopausal and perimenopausal women with HER2-negative advanced breast cancer and Verzenio (abemaciclib) for postmenopausal women with HER2-negative advanced or metastatic breast cancer being treated for the first time.

6. Less is More for Early Breast Cancer

While metastatic breast cancer remains difficult to treat, some women with early-stage breast

cancer can do well with less intensive therapy, thereby reducing side effects. The TAILORx study, presented at the American Society of Clinical Oncology annual meeting, showed that the Oncotype DX tumor gene test could enable about 70 percent of women with low-risk estrogen receptor-positive, HER2-negative early breast cancer to safely skip chemotherapy after surgery. Another study showed that taking Herceptin (trastuzumab) for six months reduced the risk of cancer recurrence and death as much as the standard 12 months of treatment with fewer cardiac side effects. But those who need post-surgery treatment shouldn't wait. A study at the San Antonio Breast Cancer Symposium showed that women with triple-negative breast cancer who delayed adjuvant chemotherapy for more than a month after surgery had a higher risk of disease recurrence and death than those who started promptly.

7. Advances in Prostate Cancer

Testosterone and other male hormones stimulate prostate tumor growth, and androgen deprivation therapy (ADT) is used to reduce testosterone production. But this may not be enough to halt disease progression. In February, the FDA approved Zytiga, (abiraterone acetate), which stops production of other androgens throughout the body. The LATITUDE and STAMPEDE studies showed that starting Zytiga early along with ADT reduced the risk of death by about 40 percent. The following week the FDA gave the nod to Erleada (apalutamide), which interferes with androgen receptor signaling. In the SPARTAN trial, Erleada delayed cancer progression or death by two years. A similar drug, Xtandi (enzalutamide)—approved in July—reduced the risk of metastasis or death by 71 percent. In April, the American Society of Clinical Oncology released new guidelines recommending that Zytiga or the chemotherapy drug docetaxel be added to ADT for men with advanced prostate cancer who haven't yet received hormone therapy.

8. HPV Vaccine Up to Age 45

In October, the FDA expanded its approval of the Gardasil 9 human papillomavirus (HPV) vaccine for women and men ages 27 to 45. The vaccine protects against nine different types of HPV, several of which can cause cervical, anal, and mouth and throat cancers. HPV is usually sexually transmitted, and the Centers for Disease Control and Prevention recommends HPV vaccination for girls and boys at age 11 or 12, before they become sexually active. The vaccine was previously available only for those up to age 26, but recent research found that many people above that age have not yet acquired all the HPV types covered by the vaccine and therefore can still benefit. Some studies show that oral carcinoma has become the most common HPV-linked cancer—and like cervical and anal cancer, the vaccine can offer protection.

9. Exercise Is Beneficial During and After Treatment

Some of this year's treatment news didn't involve medications. A growing body of evidence shows that physical activity during cancer treatment can lead to fewer side effects and better quality of life—and it may lower the risk of recurrence and cancer-related death. A meta-analysis of 34 clinical trials by the POLARIS consortium, presented at the 2018 Cancer Survivorship Symposium in February, showed that exercise significantly reduces fatigue, regardless of the type and stage of cancer. In May, the Clinical Oncology Society of Australia issued a position statement recommending that exercise be considered an important part of cancer care. The experts advised

getting at least 150 minutes of moderate or 75 minutes of vigorous aerobic exercise—such as walking, biking or swimming—and two or three sessions of resistance exercise each week.

10. Treatment Cost and Access at the Forefront

Improvements in cancer treatment can seem like a hollow victory if most patients can't benefit from them. The cost of treatment and the need for access to new therapies were frequently in the headlines in 2018. In May, President Donald Trump signed a controversial Right to Try bill that aims to make it easier for people with life-threatening illnesses to use promising experimental therapies before they complete the clinical trials. Opponents of the legislation say the FDA already approves more than 99 percent of expanded access requests and the main roadblock is companies that don't provide their drugs. Supporters argue that the expanded access process is too burdensome and few people make use of it, adding that it is also important to remove barriers to clinical trial participation for sicker patients. The financial toxicity of cancer care—especially pricey precision medicine—is a growing concern for patient, providers and politicians as studies show that people with cancer face serious financial hardship and many are willing to pay almost anything for treatment.
