Sorrento Therapeutics/MabTech have completed late-stage trials in China for STI-001, a cetuximab (Erbilux) biosimilar for the treatment of EGFR-expressing metastatic colorectal cancer, and STI-002, an infliximab (Remicade) biosimilar to treat rheumatoid arthritis. Compared with irinotecan alone, STI-001 plus irinotecan significantly improved overall response (32.9% vs. 12.8%) and progression-free survival (5.6 vs. 3.2 months) in one double-blind, randomized trial in 501 patients with colorectal cancer. The combination therapy had an overall survival advantage of 0.7 months. In the controlled study of 330 patients with rheumatoid arthritis, STI-002 administered with methotrexate demonstrated efficacy similar to infliximab, with less immunogenicity and antidrug antibody formation rates lower than those of infliximab.

Data from two Gilead Sciences-sponsored trials evaluating the use of once-daily tenofovir alafenamide (TAF) in treatment-naive and experienced adults with hepatitis B showed that TAF was noninferior to tenofovir (Viread). TAF also showed improved renal and laboratory safety parameters compared with the reference drug, which also is made by Gilead.

CHS-0214, Coherus BioSciences’ biosimilar of etanercept (Enbrel), demonstrated equivalence in a confirmatory head-to-head study in patients with moderate to severe rheumatoid arthritis. The primary efficacy endpoint was the proportion of subjects achieving ACR20 at Week 24. There were no clinically meaningful differences in the safety and immunogenicity profiles of the two products.

Hope for people with rare surgical complication
Defibrotide improved survival rates in adult and pediatric patients with hepatic veno-occlusive disease (VOD) with multiorgan failure (MOF) following hematopoietic stem-cell transplantation (HSCT). Statistically significant improvement was seen in Day 100 survival, the primary endpoint, and in rates of complete response by Day 100 compared with historical controls. The estimated difference between groups in Day 100 survival was 23%.

VOD, also known as sinusoidal obstruction syndrome, is a potentially fatal form of hepatic injury. VOD with MOF is a rare complication of HSCT, and no therapy is specifically indicated for it. Writing in the journal Blood, study investigators said the historical-control methodology offers a new approach for phase 3 evaluation of orphan diseases associated with high mortality in which a placebo control would be unethical.

OA injectable meets endpoint
FX006 (Ziletella), an investigational nonopioid/non-NSAID injectable, beat placebo in reducing moderate to severe osteoarthritis of the knee. Over 12 weeks of treatment, FX006 patients experienced pain reduction averaging 50 percent from baseline. FX006, which combines triamcinolone acetonide (TCA) with a polymer intended to provide persistent concentrations of the drug and to amplify the magnitude of pain relief, is designed to avoid serious side effects common to oral therapies, says its maker, Flexion Therapeutics.

FX006 also achieved significant improvements in stiffness and function against placebo and immediate-release TCA, but missed a secondary goal of significantly improving scores on a daily pain rating scale compared with TCA. The drug has received fast-track designation by the FDA.

Osteoporosis fracture risk lower with “romo”
Women taking Amgen/UCB’s romosozumab for osteoporosis experienced a 73% reduction in risk for spine fractures and a 36% reduction in risk for all clinical fractures compared with placebo, according to data from the FRAME study. The effect lasted through 12 months of treatment as patients were transitioned to denosumab (Prolia), but the drug didn’t reduce the incidence of nonvertebral fractures in patients who were followed for an additional year, a secondary endpoint.

The data did not match those of Radius Health’s abaloparatide, an investigational parathyroid-hormone-related protein analog, which achieved an 86% reduction in spine fracture risk compared with placebo last year. But romosozumab is injected once a month and may not need a black box warning for osteosarcoma, whereas abaloparatide is a daily injectable.

Teriparatide (Forteo), another daily injectable, carries a black box warning for osteosarcoma, whereas abaloparatide is a daily injectable.

Setback for kidney transplant agent
Chimerix ended two late-stage studies of its oral antiviral brincido-
<table>
<thead>
<tr>
<th>Date (type)</th>
<th>Manufacturer</th>
<th>Drug (trade) name; administration</th>
<th>Indication</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Jan. 28 (NDA)</td>
<td>Merck</td>
<td>elbasvir/ grazoprevir (Zepatier); oral tablet</td>
<td>For adults with chronic HCV genotypes 1 and 4</td>
<td>Efficacy and safety of this interferon-free regimen were evaluated in 6 clinical trials involving 1,373 participants with and without cirrhosis, HIV co-infection, or renal impairment. Across trials, SVR ranged from 94% to 97% in treatment groups. In about 1% of trial subjects, liver enzymes were &gt;5 times ULN at or after Week 8. $54,600 WAC may force Gilead to offer deep discounts for a similar medication, Harvoni, which goes for $94,500.</td>
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<tr>
<td>Jan. 15 (sBLA)</td>
<td>Novartis</td>
<td>ofatumumab (Arzerra); IV injection</td>
<td>Extended treatment of patients in partial or complete response after two or more lines of CLL therapy</td>
<td>New indication based on the phase 3 PROLONG trial, which showed that CLL patients on ofatumumab maintenance therapy had close to double PFS (29.4 months) vs. those on observation (15.2 months). Ofatumumab is already approved for previously untreated CLL patients for whom fludarabine-based therapy is inappropriate or who are refractory to fludarabine and alemtuzumab.</td>
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<tr>
<td>Jan. 28 (sBLA)</td>
<td>Eisai</td>
<td>eribulin mesylate (Halaven); IV injection</td>
<td>Unresectable or metastatic liposarcoma in patients who have received chemotherapy with an anthracycline</td>
<td>New orphan indication to treat a rare soft tissue sarcoma that occurs in fat cells. The first drug to show OS improvement in this population, eribulin bested dacarbazine by 7.2 months in patients with liposarcoma. In an open-label study of 446 patients with liposarcoma and leiomyosarcoma, OS gains were less impressive (2.4 months) for the entire study group, but approval was based on outcomes of the 143 patients with liposarcoma. Eribulin was originally approved in 2010 for metastatic breast cancer.</td>
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<tr>
<td>Feb. 5 (sNDA)</td>
<td>Bristol-Myers Squibb</td>
<td>daclatasvir (Daklinza); oral tablet</td>
<td>HCV genotypes 1 and 3</td>
<td>New labeling expands patient population to those with HIV-1 co-infection, advanced cirrhosis, or post-liver transplant recurrence of HCV.</td>
</tr>
<tr>
<td>Feb. 12 (sNDA)</td>
<td>Gilead</td>
<td>ledipasvir and sofosbuvir (Harvoni); oral tablet</td>
<td>HCV genotypes 1 and 4</td>
<td>New labeling expands genotype 1 patient population to include those with post-liver transplant recurrence or decompensated cirrhosis. Genotype 4 patient population expanded to include transplant recipients without cirrhosis or with compensated cirrhosis.</td>
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<tr>
<td>Feb. 19 (sNDA)</td>
<td>Pfizer</td>
<td>palbociclib (Ibrance); oral capsule</td>
<td>ER-positive and HER2-negative advanced or metastatic breast cancer</td>
<td>Patient population expanded to include women with disease progression after endocrine therapy, when taken with fulvestrant. Label revision based on PFS improvement in the PALOMA-3 trial; median PFS was 9.5 months for palbociclib + fulvestrant vs. 4.6 months for placebo + fulvestrant.</td>
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<tr>
<td>Feb. 26 (sBLA)</td>
<td>Genentech</td>
<td>obinutuzumab; (Gazyva); IV injection</td>
<td>Follicular lymphoma in patients who relapsed after, or are refractory to, a rituximab-containing regimen</td>
<td>New approval based on the phase 3 GADOLIN study. Patients given obinutuzumab plus bendamustine followed by obinutuzumab alone had a 52% reduced risk of disease worsening or death than patients who were treated with bendamustine alone.</td>
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CLL=chronic lymphocytic leukemia, ER=estrogen receptor, HCV=hepatitis C virus, IV=intravenous, NDA=new drug application, OS=overall survival, PFS=progression-free survival, SVR=sustained virologic response, sBLA=supplemental biologics license application, sNDA=supplemental new drug application.

Sources: American Society of Clinical Oncology, BioPharma Dive, FDA, Fierce Biotech, FixHepC.com, Lancet Oncology, Optum Rx, and manufacturer news releases and product labeling.
A reduced rate of non-CMV DNA viruses, such as BK. But an antiviral effect was seen at Week 14, with patients who received brincidofovir experiencing fewer clinically significant CMV infections than those given placebo. Chimerix plans to continue testing brincidofovir for efficacy against serious adenovirus infections and smallpox.

**Highlights from ASCO GI and GU cancer symposia**

Selected presentations from the American Society for Clinical Oncology’s January genitourinary and gastrointestinal cancer symposia:

- The novel 

  Lutetium-DOTATATE (Lutathera) demonstrated a 79% decreased risk of cancer progression or death compared with octreotide LAR for patients suffering from a rare form of cancer, advanced midgut neuroendocrine tumors, according to the phase 3 NETTER-1 trial. Lutathera is one in an emerging group of treatments called peptide-receptor radionuclide therapy, which target carcinoid tumors with radiolabeled somatostatin analogue peptides.

- Adding evofosfamide to gemcitabine in patients with metastatic pancreatic cancer did not provide an overall survival (OS) advantage, according to the phase 3 MAESTRO trial, nor did it show a significant OS improvement over gemcitabine alone (8.7 vs. 7.6 months).

- Findings from the randomized phase 2/3 SCOPE 1 trial show that chemoradiotherapy with or without cetuximab (Erbitux) in patients with esophageal cancer yielded a 3-year OS rate of 47.2% in the chemoradiotherapy alone arm, which is comparable to data from surgical trials. Investigators called the result unprecedented.

- Panitumumab (Vectibix) and best supportive care (BSC) may significantly improve OS in patients with chemorefractory wild-type KRAS metastatic colorectal cancer, compared with BSC alone. These phase 3 findings were the first to analyze panitumumab efficacy by wild-type KRAS (exon 2) and wild-type RAS tumor mutation status, providing information about OS in new subpopulations.

- New analysis of phase 3 CheckMate-025 data showed that nivolumab (Opdivo) as second-line therapy for patients with advanced renal cell carcinoma (RCC) achieved consistent objective response and OS across subgroups. Versus everolimus (Afinitor), nivolumab performed better across baseline factors such as Karnofsky performance status, Heng risk criteria, or number of prior therapies regardless of prior treatment with sunitinib (Sutent) or pazopanib (Votrient).

- Patients with advanced RCC treated with cabozantinib (Cometriq) had a median progression-free survival of 7.4 months compared with 3.9 months for patients treated with everolimus, according to an interim analysis of the phase 3 METEOR trial. Using the MSKCC risk-assessment criteria, 43% of patients had favorable-risk disease, 41% had intermediate-risk disease, and 15% had poor-risk disease.

**Long-term studies in CML**

Five-year results of the randomized ENESTnd trial show a positive risk-benefit profile for nilotinib (Tasigna) compared with imatinib (Gleevec) in patients with chronic myeloid leukemia (CML). Cardiovascular risk was slightly higher with nilotinib, but improvements in CML disease control could outweigh those risks. By the end of Year 5, 217 patients (77%) in the lower-dose (300 mg twice daily) and 217 patients (77%) in the higher-dose (400 mg twice daily) nilotinib groups achieved a major molecular response, versus 171 (60%) imatinib patients (400 mg once daily). Progression to accelerated or blast phase was more likely with imatinib.

**Have you heard?**

In an important application of drug repurposing—a topic covered elsewhere in this issue of Managed Care—results from the large STAMPEDE trial suggest that a bisphosphonate and a COX-2 pain reliever may prevent tumor regrowth in some patients with prostate cancer. In patients whose disease had metastasized, a combination of zolezronic acid and celecoxib had a median of 22 months of treatment-failure-free survival, compared with 19 months in a group that received standard of care. The 5-year failure-free survival rates were 29% and 26%, respectively. The results were statistically significant. The data suggest that inhibition of COX-2 with agents such as celecoxib could inhibit the growth and invasiveness of prostate cancer cells, and epide-miologic studies have suggested a protective effect against prostate cancer from nonsteroidal anti-inflammatory drugs.

— Katherine T. Adams

*All clinical studies mentioned in this article are phase 3 unless otherwise stated.*