Hopes raised, hopes dashed — the last half of 2012 has seen plenty of both. Enthusiasm over a bumper crop of U.S. Food and Drug Administration approvals has been tempered by a long list of phase 3 trial disappointments.

Oncology agents led the way, starting with two drugs being studied for the treatment of non-small cell lung cancer. The addition of Eli Lilly’s pemotrexed (Alimta) to a regimen of bevacizumab (Avastin) and chemotherapy produced improvements in progression-free survival (PFS) but not overall survival (OS). ArQule and Daiichi Sankyo stopped a phase 3 study of tivantinib after concluding that improvements in OS would not be reached. For ArQule, the silver lining was the FDA’s grant of a special protocol assessment, allowing the start up of a phase 3 trial of tivantinib in patients with liver cancer.

Amgen ended a large phase 3 trial of ganitumab after a data monitoring committee determined that the addition of ganitumab to gemcitabine (Gemzar) would not result in significant OS improvements in patients with pancreatic cancer versus gemcitabine alone. A phase 2 trial of ganitumab in locally advanced pancreatic cancer was also stopped.

Two separate studies of agents to treat kidney cancer also caused consternation. Temsirolimus (Torisel), currently on the market for advanced renal cell carcinoma, was no better at extending PFS when combined with bevacizumab than a combination of bevacizumab and interferon alfa-2a. And Aveo is reevaluating data from a head-to-head trial of its tivozanib versus sorafenib (Nexavar) after the FDA expressed concern about OS data that Aveo planned to include in a new drug application later this year.

Not all news from oncology was disappointing. Immunogen released a deeper dive into OS data for trastuzumab emtansine, or T-DM1 (Kadcyla), showing a 5.8-month OS benefit in previously treated HER2-positive metastatic breast cancer patients versus lapatinib (Tykerb) plus capecitabine (Xeloda). And Celgene’s multiple myeloma oral drug, pomalidomide — a derivative of thalidomide — improved PFS in patients who were refractory to lenalidomide (Revlimid) and bortezomib (Velcade).

Alzheimer’s data quandary
Is half a loaf better than nothing? That seems to be the message from researchers who conducted two large studies of solanezumab, Eli Lilly’s experimental Alzheimer’s agent. Solanezumab missed its primary endpoint in two pivotal trials, but in a subsequent analysis, researchers found a biomarker they say opens a new avenue for Alzheimer’s research.

As Lilly mulls whether to pursue FDA approval on secondary data, observers raise questions: Will the FDA require another phase 3 trial to validate the biomarker theory? Or will the agency be willing to accept substandard data to help Alzheimer’s patients cope as best as they can with a disease for which no effective therapies exist? The questions loom larger in the wake of Janssen and Pfizer’s announcement on Aug. 6 that they had pulled the plug on development of an IV formulation of another hyped Alzheimer’s treatment in late-stage development, bapineuzumab.

MS drugs take spotlight
Biogen Idec steamed toward approval of its oral MS agent, BG-12, with publication of two pivotal studies in the New England Journal of Medicine. In both the DEFINE and CONFIRM studies, the primary endpoint (reductions in relapse rates) was reached with ease. Safety profiles were favorable in both studies as well, bolstering the perception among patient advocates that BG-12 may have come as close as anything to bridging the efficacy/safety tradeoff that defines MS therapies. In DEFINE, BG-12 was compared to placebo; in CONFIRM, glatiramer acetate (Copaxone) was a comparator drug.

On BG-12’s heels, Sanofi and Genzyme published positive data from two pivotal trials of alemtuzumab (Lemtrada) in the Lancet. In both, alemtuzumab was significantly more effective at reducing
annualized relapse rates than the active comparator, interferon beta-1a (Rebif).

Both drugs, along with the approval of teriflunomide (see table) and others in development (see article on page 24) usher in a new phase of MS treatment.

Did you hear?

Sloan Kettering officials wrote in the New York Times that the cancer center won’t give patients ziv-aflibercept (Zaltrap) because of its $11,000 a month price. ... Teva and Samsung have given up trying to reproduce rituximab, ending those biosimilar programs.

All clinical trials described in Drug Track are phase 3, randomized, controlled studies unless otherwise specified.