Finding the Best Candidates for Platinum-Based Chemotherapy

Platinum-based chemotherapy is effective in metastatic triple-negative breast cancer (mTNBC), but predictive biomarkers would help identify the best candidates for the treatment. Two sets of parameters—neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR)—have demonstrated prognostic prowess in many malignancies, but how well do they perform in platinum-treated mTNBC patients? Researchers from Fondazione IRCCS Istituto Nazionale dei Tumori in Milan, Italy, conducted a retrospective, single-center study to evaluate the association between baseline NLR or PLR and progression-free survival (PFS) in 57 mTNBC patients treated with carboplatin-paclitaxel or carboplatin-gemcitabine between 2007 and 2017, compared with 148 patients with hormone receptor-positive, HER2-negative metastatic breast cancer.

Response was assessed every three chemotherapy cycles. Among platinum-treated patients, high NLR and PLR were associated with significantly lower PFS. Median PFS was 304 days in patients with an NLR of less than 2.5 and 158 days in patients with an NLR of 2.5 or greater. PFS was longer in patients with a baseline PLR of less than 200 compared with a PLR of 200 or greater. The researchers found no significant association between NLR or PLR and the PFS of control patients.

When the same parameters were evaluated before the administration of the third treatment cycle, an NLR below 2.5 was still associated with reduced risk of disease progression, although a PLR below 200 was not. In mTNBC patients, median overall survival (mOS) was significantly longer in patients with an NLR below 2.5 compared with an NLR of 2.5 or greater. PLR values were not associated with mOS. The ratios also appeared to have a generally prognostic role independent from tumor biology.

The hazard ratios for NLR and PLR in multivariable analysis for PFS were similar, and the parameters correlated with each other, the researchers say, suggesting that both NLR and PLR “well reflect the inflammatory/immune contexture in mTNBC, and may be redundant as predictive biomarkers.”

Source: *Scientific Reports*, June 2018

Testicular Pain Leads To a Unique Diagnosis

A young man presented with right testicular pain and a right epididymal mass. It was a challenge to diagnose the cause—until he revealed essential clues.

The differential diagnosis included testicular malignancy and lymphoma. However, tumor markers were within normal limits. Tests for human immunodeficiency virus (HIV) and syphilis were negative. The clinicians also considered granulomatous or chronic orchitis, but after treatment with nonsteroidal anti-inflammatory drugs, the pain and palpable epididymal mass had resolved. Then, follow-up testicular ultrasound images showed new diffuse heterogeneous hypoechoic lesions in the right testis.

The patient elected to have a right radical orchiectomy, with sperm cryopreserved. He recovered well, and semen analysis did not show any abnormalities.

Pathology of the surgical specimen revealed necrotizing and non-necrotizing granulomas. At this point, the patient recalled that he had developed cervical lymphadenopathy and oral ulcers several weeks after traveling to South America, eight months before presenting with the testicular symptoms.

Combined with another clue—frequent exposure to cats during his South America trip—his symptoms created a clearer picture. He had been diagnosed with toxoplasmosis at the time but had not received treatment because he was immunocompetent. His symptoms had resolved spontaneously, and he said he had been in his usual health between then and the development of testicular pain.

Based on this new information, the clinicians conducted immunohistochemical tests, which revealed isolated cysts approximately 20 micrometers in diameter, confirming a diagnosis of testicular toxoplasmosis. They started him on systemic toxoplasmosis treatment; he has been in good health since then.

The clinicians note that toxoplasmosis is highly prevalent, infecting up to 30% of the world’s population. Cat feces is one source of infection with *Toxoplasma gondii*, which is typically asymptomatic. In immunocompetent patients, it tends to present as an acute infection that is benign and self-limited.

Only a few cases of testicular toxoplasmosis have been reported in the literature, and all have been in immunocompromised patients. The fact that this patient was immunocompetent makes him unique—the only such case reported to date. Given the immunocompetence, the clinicians say, their patient demonstrates the need for a high index of suspicion.

Source: *BMJ Case Reports*, June 2018

Are We Beating Cancer—Finally?

Cancer death rates continue to decline in the United States in all major racial and ethnic groups, according to the latest National Cancer Institute (NCI) *Annual Report to the Nation on the Status of Cancer*. The data are an “encouraging indicator of progress” in cancer research, says NCI Director Ned Sharpless, MD. “It’s clear that interventions are having an impact.”

Overall cancer incidence dropped by 1.8% in men and 1.4% in women from 1999 to 2015. Between 2011 and 2015, death rates dropped for 11 of the 18 most common cancer types in men and 14 of the 20 most common types in women. The researchers say the “significant declines” also hold “significant differences” in rate by sex, race, and ethnicity. For example, African-American men and white women had the highest incidence rates, and African-American men and women had the highest death rates.

However, over the same period, death rates for cancers of
the liver, pancreas, and brain and nervous system rose in both men and women. Death rates for cancer of the uterus rose (the researchers say obesity is thought to be a contributing factor), and death rates for cancers of the oral cavity and pharynx and soft tissue increased in men, perhaps associated with human papillomavirus infection.

In a companion study, researchers who explored prostate cancer trends in more detail found overall incidence rates declined an average of 6.5% each year between 2007 and 2014, from 163 new cases per 100,000 men to 104 new cases. Still, after a two-decade-long steady decline, rates leveled off. Incidence of distant disease rose from 7.8 new cases per 100,000 to 9.2, but there was no increase in the rates of cases with aggressive histological grade.

Interestingly, the researchers also report a decline in recent prostate-specific antigen (PSA) screening between 2010 and 2013 national surveys. “The increase in late-stage disease and the flattening of the mortality trend occurred contemporaneously with the observed decrease in PSA screening,” said Serban Negoita, MD, DrPH, of NCI’s Surveillance Research Program. However, while “suggestive,” Dr. Negoita adds, their observation does not demonstrate causality: Many factors contribute to incidence and mortality, such as improvements in staging and treating cancer.

Source: National Cancer Institute, May 2018

Diagnostic Dilemma: When Serology Tests Are Misleading

The number of reported tick-borne diseases more than doubled between 2004 and 2016, according to the Centers for Disease Control and Prevention, and such cases now account for more than 60% of all reported mosquito-borne, tick-borne, and flea-borne disease. That’s one reason why it is important to know that a patient has spent time in a tick-promoting environment. Clinicians from Lehigh Valley Health Network Pocono and Geisinger Commonwealth School of Medicine in Pennsylvania reported on a patient whose diagnosis turned on that fact.

Their patient, a 71-year-old man, had had fever, weakness, headaches, near syncope, and nausea for four days. He also hadn’t been eating well. A complete blood count showed pancytopenia with an excess of band cells, an indicator of inflammation and infection. His aspartate transaminase levels were elevated. The diagnostic dilemma centered on these findings: Serology tests for HIV-1 and HIV-2 were positive and a peripheral blood smear showed 0.5% parasitemia consistent with Babesia microti. Both babesiosis and HIV were among the possible diagnoses.

Two important factors the clinicians had to consider: He had recently been bitten by ticks, and he was gay.

The clinicians note that a variety of infections can lead to false-positive HIV serology, such as malaria, Mycobacterium tuberculosis or Rickettsia species, influenza, and hepatitis B vaccinations. Moreover, the Ixodes tick, the same vector that transmits Borrelia burgdorferi, which causes Lyme disease, also transmits B. microti. Conversely, HIV infection can exacerbate Lyme disease or babesiosis.

The tests showing B. microti were the clincher for the clinicians, who started treatment with fluids, atovaquone, and azithromycin. The patient recovered completely. Repeat HIV serology was negative.

The authors of the report note that babesiosis can be a life-threatening infection in patients with reduced immunity. It’s possible that, like malaria and HIV serologies, Babesia and HIV serologies cross-react, the clinicians say. Thus, it’s important to screen for both in both infections.

Theirs is the first case, to their knowledge, of a false positive result for HIV associated with active babesiosis.

Source: BMJ Case Reports, June 2018

Tick, Tick, Tick

As if it weren’t bad enough that illnesses from mosquito, tick, and flea bites tripled between 2004 and 2016, nine new germs spread by mosquitoes and ticks were discovered or introduced into the U.S. in the same 13 years.

According to the first summary by the Centers for Disease Control and Prevention (CDC) collectively examining data trends for all nationally notifiable diseases caused by the bite of an infected mosquito, tick, or flea, the most common tick-borne diseases in 2016 were Lyme disease and ehrlichiosis/anaplasmosis. The most common mosquito-borne viruses were West Nile, dengue, and Zika.

The increase is due to many factors, the CDC says, but one issue is that mosquitoes and ticks are moving into new areas, putting more people at risk.

The U.S. is “not fully prepared” to meet the public health threat, the CDC warns: About 80% of vector-control organizations lack critical prevention and control capacities. Reducing the spread of the diseases and responding effectively to outbreaks will require additional capacity at the state and local levels for tracking, diagnosing, and reporting cases.

Source: CDC, May 2018

Acute Hepatitis E Superinfection Reactivates Chronic Hepatitis B

Many things can reactivate chronic hepatitis B—withdrawal of antiviral therapy, pregnancy, and chemotherapy, to name a few. So when a patient with stable chronic hepatitis B presented with a significant hepatitis flare, clinicians from Beth Israel Deaconess Medical Center in Boston had a long list to check.

They first ruled out drug-associated hepatotoxicity and screened the patient for common causes of acute hepatitis. Beyond the hepatitis B, she did not have other significant medical conditions, had not had close contact with anyone...
who was ill, and was not pregnant. Tests were negative for cytomegalovirus, Epstein-Barr virus, HIV, and hepatitis A, C, and D. She had tested negative for anti-hepatitis E virus (HEV) immunoglobulin M and G in a visit about nine months before.

However, she reported regularly consuming pork. Thus, the clinicians focused on hepatitis E serology, which confirmed that she had an acute HEV infection.

Pigs act as a “natural reservoir” for HEV; contaminated meats and direct contact with animals are the most common causes of HEV human infection in industrialized countries. Recent data reveal the prevalence of HEV antibodies in the U.S. is around 6%, illustrating that it is not as uncommon as it was thought to be. Although there was no direct evidence to confirm the source of the patient’s infection, it seemed likely due to pork consumption. She was started on tenofovir, but stopped it four months later because she felt well. After a subsequent flare, “repeated counseling” persuaded her to start on entecavir, with successful viral suppression.

Hepatitis E superinfection with chronic hepatitis B can contribute to significant morbidity and mortality, the clinicians say, particularly in patients with cirrhosis. Concurrent infection with another viral hepatitis should be considered in both immunodeficient and immunocompetent patients with chronic hepatitis B reactivation.

Source: BMJ Case Reports, June 2018

Combination Treatment Prevents Stroke

Combining clopidogrel and aspirin following a small stroke or minor stroke symptoms reduces the risk of a new stroke, heart attack, or other ischemic event within 90 days, according to researchers from the National Institute of Neurological Disorders and Stroke (NINDS).

In POINT (Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke), an international clinical trial of nearly 5,000 patients, 5% of the combination therapy group and 6.5% of the aspirin-only group had an ischemic event within 90 days. The benefit of the combination was concentrated in the first two weeks, while the risk of bleeding was constant over 90 days, says NINDS Director Walter Koroshetz, MD, so the treatment may be most valuable in acute management of a minor ischemic stroke or TIA.

The study was stopped early not only because the combination therapy was more effective than aspirin alone in preventing severe strokes, but also because of the risk of severe hemorrhage. The combination therapy was associated with an increase in major bleeding, although many of the episodes were not fatal and occurred outside the brain: 0.9% of the combination group had a major hemorrhage, compared with 0.4% of the aspirin-only group. “Overall, the risk of severe bleeding was very small,” says lead investigator S. Claiborne Johnston, MD, PhD, “but it was not zero.”

Source: National Institutes of Health, May 2018

Suicides on the Rise

African-American children 5 to 12 years of age are roughly twice as likely as white children to commit suicide, according to a study funded by the National Institute of Mental Health. But that trend reverses in adolescence: From ages 13 to 17, the suicide rates for white children are double those of black children.

The researchers used the Web-based Injury Statistics Query and Reporting System of the Centers for Disease Control and Prevention (CDC) to analyze data from 2001–2015 separately for each age group. The data were limited, the researchers say, and did not include information on contributing factors. Study findings highlighted the need for a greater understanding of age-related racial disparities in youth suicide.

The disturbing findings are part of an overall rise in suicide nationwide. Suicide is the 10th leading cause of death in the U.S., according to the latest CDC figures. In 2016, nearly 45,000 Americans 10 years of age or older died by suicide.

In 2017, the CDC released Preventing Suicide: A Technical Package of Policy, Programs, and Practices, with evidence-based strategies (www.cdc.gov/media/releases/2018/p0607-suicide-prevention.html). The strategies include creating protective environments by reducing access to lethal means among at-risk individuals and intervening at “suicide hotspots” by, for example, putting barriers on tall structures. “Like most public health problems,” the guide says, “suicide is preventable.”

Sources: National Institute of Mental Health, May 2018; CDC, 2017

Concussion Patients Aren’t Getting Enough Follow-Up

Many patients with traumatic brain injury (TBI) may not be receiving follow-up care, according to findings from Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI), a long-term study funded by the National Institutes of Health.

Of 831 patients who completed questionnaires two weeks and three months after sustaining TBI, 44% reported seeing a health care provider within three months. Of those, 15% visited a clinic that specialized in head injury. Approximately half saw a general practitioner; close to a third reported seeing more than one type of doctor.

Among the 279 patients with three or more symptoms of moderate-to-severe post-concussion, 41% had not had a follow-up visit at three months. Moreover, half of the patients were discharged without TBI educational materials.

Rates and components of follow-up care varied widely from institution to institution, even among patients with the same initial degree of injury.

Source: National Institutes of Health, May 2018
**Swim at Your Own Risk**

Hotel pools and hot tubs are breeding grounds for waterborne bacteria—and they can be deadly. Between 2000 and 2014, germs spread through treated recreational water caused at least 27,219 illnesses and eight deaths.

According to a study by the Centers for Disease Control and Prevention (CDC), efforts to prevent outbreaks have had mixed results. The number of Legionella-related respiratory disease outbreaks increased over time, while Pseudomonas-related skin infection outbreaks declined and Cryptosporidium-related diarrheal disease outbreaks leveled off.

**Legionella**, which can cause severe pneumonia and flu-like symptoms, was responsible for 16% of outbreaks. Another 13% were due to Pseudomonas, which can cause “hot tub rash” and swimmer’s ear. When a pool, hot tub, or water playground isn’t cleaned properly, bacteria grow and form biofilm on wet surfaces, ideal growing grounds for bacteria like Legionella and Pseudomonas. It is harder for disinfectants to kill these bacteria when they are protected by biofilm, the CDC says.

The worst offender was Cryptosporidium, which caused 58% of the outbreaks and 89% of the illnesses. “Swallowing just a mouthful of water with Crypto in it can make otherwise healthy kids and adults sick for weeks,” said Michele Hlavsa, RN, MPH, chief of the CDC’s Healthy Swimming Program. Chlorine can’t kill Cryptosporidium quickly, she cautions. The best way to avoid it is to keep it out of the water in the first place. That means keeping anyone (usually young children) with gastrointestinal problems or diarrhea out of the pool.

Other CDC tips: Check the inspection scores for pools, hot tubs, and water playgrounds; use a test strip from a pool supply store to check the pH and bromine or free chlorine levels; don’t swallow pool water; take kids on regular bathroom breaks; and change diapers in the diaper-changing area, away from the water.

Source: CDC, May 2018

**Former Smokers Motivate Quitters**

In 2012, the Centers for Disease Control and Prevention (CDC) launched the “Tips From Former Smokers” campaign. It was memorable and emotionally forceful—one woman who had oral and throat cancer delivered her ad through an artificial voicebox—but did it have an impact on quitting rates?

CDC researchers looked at sustained (six month) cigarette abstinence between the first four years of the campaign (2012–2015). They found that the Tips campaign led to about 522,000 sustained quits. The comprehensive approach combining evidence-based messages with the promotion of cessation resources was highly successful. Their finding of more than half a million sustained quits underscores the critical role of national tobacco education campaigns as a “counterpoint” to substantial pro-tobacco advertising and promotion.

Source: *Preventing Chronic Disease*, May 2018

**Rare Hepatitis A Outbreak in a Childcare Facility**

In young children, hepatitis A is usually asymptomatic. So a childcare facility in Ireland was taken off guard by an outbreak of hepatitis A that infected seven adults and five children, putting six of the adults in the hospital. By the time the investigation and interventions were over, more than 554 contacts had been followed up, and it had all cost more than 45,000 Euros (about $52,000).

The outbreak was traced to a man with hepatitis A whose child had been unwell for three weeks with fever, fatigue, abdominal pain, diarrhea, pale stools, and possible jaundice. The child (and a cousin, also infected) attended a local childcare facility, but because several other cases seemed to be limited to the family and their friends, no one immediately considered the facility as a possible source of infection. However, approximately 10 days after the first two cases were reported, an outbreak was officially declared at the facility.

At the time, 93 children were attending the facility. All seven adults were household contacts of children in the facility.

As many as 70% of infections are asymptomatic in children younger than 6 years of age, the researchers note, but that group is often a source of transmission as a result of suboptimal hygiene. Transmission is usually fecal-oral and person-to-person. Although the initial source of the outbreak was not identified, the subsequent transmission suggested person-to-person spread. The researchers say the distribution of cases suggests that the transmission probably happened in the school, with asymptomatic children infecting their families—highlighting the fact that symptomatic cases of hepatitis A represent only a proportion of cases in an outbreak.

A preschool inspection report that preceded the outbreak highlighted deficiencies in the staff’s handwashing practices. An infection control audit undertaken because of the outbreak found a number of deficits, including lack of foot-operated bins and the use of cloth covers on furnishings rather than waterproof material.

Medical expenses, including hospitalization, serology, and vaccine, cost between 43,400 and 47,400 Euros ($50,500 to $55,200).

The researchers say the delayed notification to public health officials of the first case probably contributed to the extent of the outbreak. Medical professionals, they note, should be aware that, while uncommon, hepatitis A still occurs. Prompt recognition and notification can mitigate the significant morbidity associated with the infection.

Source: *Epidemiology and Infection*, April 2018