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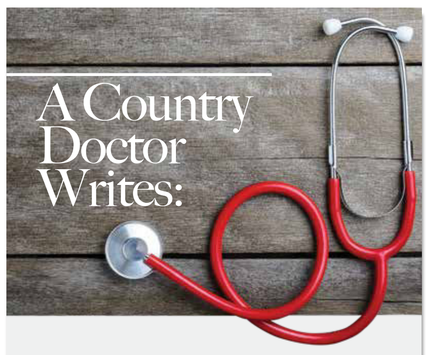


Meaningful Us

Meaningful Use was a vision for EMRs that in many ways turned out to be a joke. Consider my list of Meaningful Us for medical professionals instead.

When electronic medical records became mandatory, federal monies were showered over the companies that make them by way of inexperienced, ill-prepared practices rushing to pick their system before the looming deadline for the subsidies.

The feds tried to impose some minimum standards for what EMRs should be able to do and for what practices needed to use them.

The collection of requirements was called meaningful use, and by many of us, nicknamed "meaningless use." Well-meaning bureaucrats with little understanding of medical practice wildly overestimated what software vendors—many of them startups—could deliver to such a well-established sector as healthcare.

For example, the feds thought these startups could produce or incorporate high-quality patient information that we could generate via the EMR, when we have all built our own repositories over many years of practice from Harvard, the Mayo Clinic, and the like or purchased expensive subscriptions like UpToDate. As I have described before, I would print the hokey EMR handouts for the meaningful use credit and throw them in the trash and give my patients the real stuff from UpToDate, for example.

I'd like to introduce an alternative set of standards, borrowing the hackneyed phrase, with a twist. **Meaningful Us for Medical Professionals:**

Unbiased, Understanding, Unflappable, Unhurried

Like the software meaningful use items, these may be hard to attain, but especially in today's healthcare environment, they seem worthy of striving for.

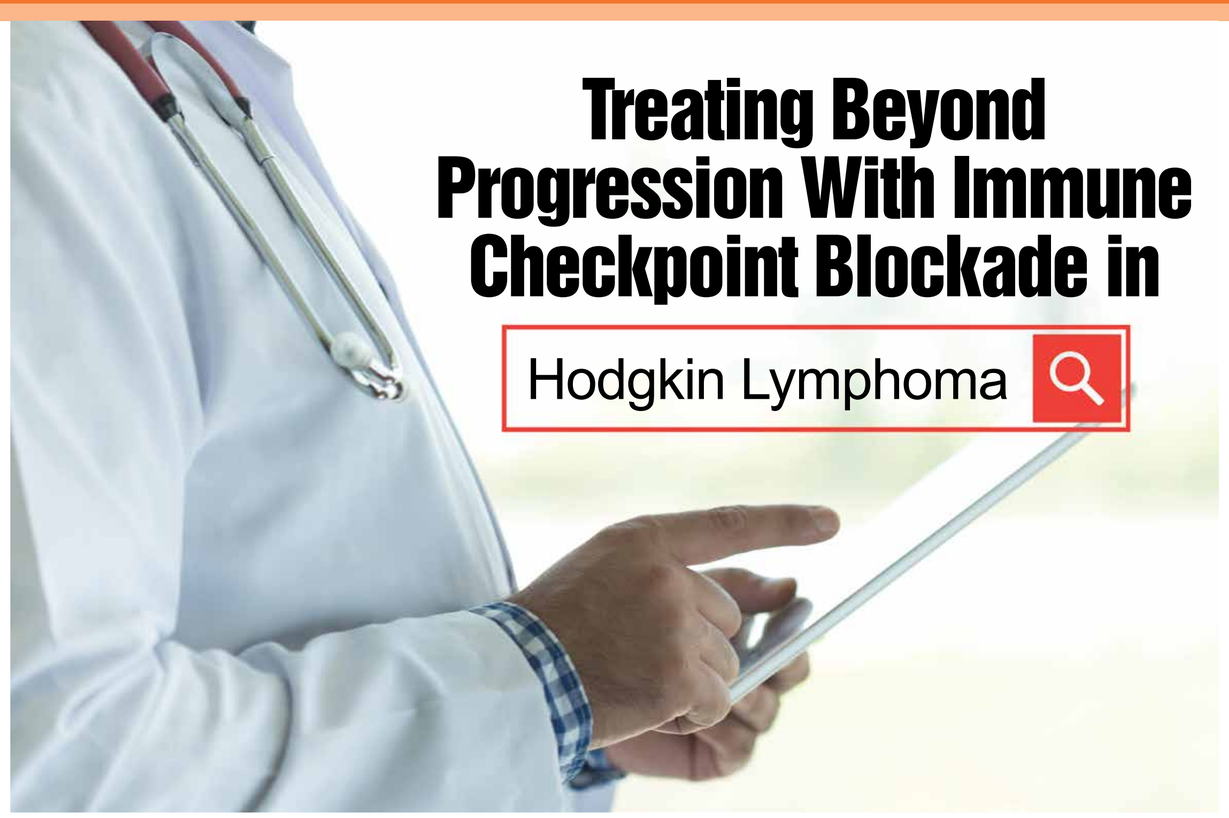
UNBIASED
Able to fairly represent alternative approaches to allow patients to make up their own mind about their care.

UNDERSTANDING
Able to listen to patients' concerns and reflect back that you "get it" and will work to help address them.

UNFLAPPABLE
Able to, in Osler's words, maintain equanimity in the face of the challenges of medical practice.

UNHURRIED
Able to use time wisely, therapeutically, without frenzy, to make the most of the most valuable resource we all have.

Now, isn't that more inspiring?



Treating Beyond Progression With Immune Checkpoint Blockade in Hodgkin Lymphoma

Contributor
Reid W. Merryman, MD
Physician
Instructor in Medicine
Dana Farber Cancer Institute

The treatment landscape in Hodgkin lymphoma (HL) has changed significantly in recent years with the FDA approval of two immune checkpoint blockade (ICB) therapies, and more of these agents are also being tested in HL. "Across multiple tumor histologies, including HL, oncologists have recognized that some patients treated with ICB therapies will experience atypical response patterns," explains Reid W. Merryman, MD. "For example, some patients may have imaging evidence of progression, but with continued ICB treatment, they later achieve a response or durable disease control."

Provisional modifications of response criteria have been proposed to permit continued use of programmed cell death-1 (PD-1) monoclonal antibodies (mAbs) or other ICB therapies beyond conventionally defined progression. Despite these criteria, data are lacking on the potential benefits of treatment beyond progression (TBP) in HL.

For a study published in *The Oncologist*, Dr. Merryman, and colleagues collected data from patients with relapsed or refractory HL who received ICB treatment across 17 academic centers. They reviewed medical records from 64 patients with HL who received standard-of-care or investigational ICB agents and at least one subsequent therapy and progressed while receiving their treatment regimen. In total, 20 patients received TBP (TBP cohort) and 44 stopped ICB therapy at initial disease progression (non-TBP cohort). "Our goal was to characterize outcomes of TBP and its impact on subsequent treatments," says Dr. Merryman.

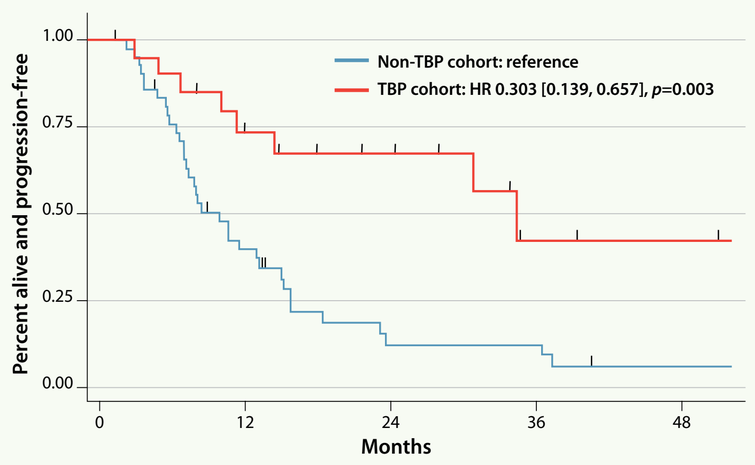
Highlighting Key Findings

Among patients who received TBP, the researchers examined possible predictors of time-to-next treatment (TTNT), which was defined as time from initial progression on ICB therapy to initiation of a subsequent treatment. Patients who received ICB therapy for longer than 4.7 months prior to initial progression had longer TTNT than those treated for fewer than 4.7 months before initial progression. "Patients receiving TBP rarely achieved an objective response, but many had durable disease control," Dr. Merryman says. "In fact, 35% of patients receiving TBP did not require a subsequent therapy for more than 1 year. Not surprisingly, we also found that the TTNT was longer for patients in the TBP cohort than for the non-TBP cohort (6.6 months vs 1.4 months)."

Continuing an ineffective therapy beyond progression could have a negative impact on the efficacy of subsequent treatments. As such, the overall response rate and progression-free survival (PFS) of post-ICB treatment was analyzed. Overall and complete response rates to post-ICB treatments were similar for the TBP and non-TBP cohorts. "However, patients in the TBP cohort had improved PFS with subsequent treatment," says Dr. Merryman. PFS of post-ICB therapy was actually longer in the TBP cohort than the non-TBP cohort, with a median of 17.5 months vs 6.1 months, respectively.

In addition, the investigators assessed time to subsequent treatment failure (TTSTF), which was defined as time from initial ICB progression to failure of subsequent treatment. "Patients in the TBP cohort had significantly longer TTSTF than those in the non-TBP cohort (34.6 months vs 9.9 months)," Dr. Merryman says (Figure). "This benefit persisted even after controlling for several potential confounding variables, including the type of treatments patients received after ICB, symptoms at the time of progression, and subsequent transplantation."

Figure Time to Subsequent Treatment Failure



Abbreviation: EPIT, epicutaneous immunotherapy; HRQOL, health-related quality of life; OIT, oral immunotherapy.

Source: Adapted from: Merryman RW, et al. *Oncologist*. 2020 Apr 10 [Epub ahead of print].

More to Come

Data from the analysis must be confirmed in future research because of the study's retrospective design, according to Dr. Merryman. "In the meantime," he says, "our data suggest that TBP with a PD-1 monoclonal antibody may be a beneficial strategy for selected patients with HL. This strategy might be considered for patients who are clinically stable with asymptomatic progression. Importantly, based on LYRIC criteria, patients receiving TBP should undergo a repeat imaging assessment 8-12 weeks after initial progression to monitor treatment response."

Dr. Merryman notes that future studies should test the strategy of TBP in a prospective fashion with well-defined eligibility criteria to learn more about the potential benefits of TBP. "Obviously, the ideal approach to clarify the benefits of TBP would be a randomized trial, but this will be challenging to conduct in this relatively small patient population," he says.

In Case You Missed It

Good Diet May Cut Toxicity Risk in Treatment of Pediatric ALL

Diets high in antioxidant-rich foods may cut the risk of developing bacterial infections or mucositis during the first phase of acute lymphoblastic leukemia (ALL) treatment in pediatric patients, according to a study published in the *Journal of Clinical Oncology*. Researchers analyzed clinical and dietary survey data from 513 children with ALL participating in a prospective clinical trial. Associations between dietary intake of antioxidants and treatment-related toxicities and survival were evaluated both in the induction and post-induction phases of therapy. The study team found that 23% and 16% of patients experienced a bacterial infection during the induction or post-induction phases of treatment, respectively, while 4% and 10%, respectively, experienced mucositis. There was a significant association noted between increased intake of dietary antioxidants and lower rates of infection and mucositis. There were no associations seen between dietary antioxidants and either relapse or disease-free survival. Additionally, the investigators observed no associations between supplementation and toxicity, relapse, or survival. "This is the first study to suggest that a high-quality diet, rather than taking supplements, during ALL treatment may be beneficial in reducing these common toxicities," a coauthor said in a statement.

In AML, Time From Diagnosis to Treatment Not Linked to Survival

For patients with newly diagnosed acute myeloid leukemia, the time from diagnosis to treatment start (TDT) for intensive treatment is not associated with overall survival, according to a study published in *Blood*. Study investigators selected 2,263 acute myeloid leukemia patients with intensive induction treatment and a minimum follow-up time of 12 months to examine the influence of TDT on remission, early death, and overall survival. Patients with TDT of longer than 50 days were excluded from the analysis. The median TDT was 3 days. For TDT of 0-5, 6-10, 11-15, and more than 15 days, the unadjusted 2-year overall survival rates were 51%, 48%, 44%, and 50% percent, respectively. The hazard ratio for TDT as a continuous variable was 1.00 in a multivariable analysis accounting for established prognostic variables. No significant between-group differences were seen when overall survival was analyzed separately and stratified for age of 60 or older versus younger than 60 and for high versus low initial white blood cell count. "In the majority of patients, it seems safe to wait for the diagnostic results in order to assign the patient to the correct subgroup and select the appropriate treatment, rather than using the historic one-size-fits-all chemotherapy approach," a co-author said in a statement. "We think a potential deterioration in prognosis, if it exists at all, will be much smaller than the clinical benefit a patient would gain by receiving the appropriate novel treatment."

Poor Outcomes With Common NHL Conditioning Regimen

In patients with non-Hodgkin lymphoma (NHL) undergoing allogeneic hematopoietic cell transplant (HCT), treatment with a more intense reduced-intensity conditioning and nonmyeloablative conditioning (RIC-NMAC) regimen—such as fludarabine-melphalan (Flu-Mel140), the most commonly used of these regimens—may negatively affect overall survival (OS) and be associated with higher non-relapse mortality, according to study results published in *JAMA Oncology*. In addition, lower intensity RIC-NMAC regimens of fludarabine-intravenous busulfan (Flu-Bu) and fludarabine-cyclophosphamide (Flu-Cy) with or without 2 Gy total body irradiation (2GyTBI) brought about comparable results in OS.

Nilanjan Ghosh, MD, PhD, and colleagues assessed 1,823 adult patients with NHL who underwent allogeneic HCT to determine whether RIC-NMAC regimens of higher intensity were associated with increases in non-relapse mortality and lower OS compared with lower intensity regimens. Patients were randomized to treatment with Flu-Bu (~6.4 mg/kg), Flu-Mel140 (140 mg/m2), Flu-Cy, or Flu-Cy with 2Gy TBI (Flu-Cy-2GyTBI).

Patients treated with Flu-Mel140 compared with Flu-Bu had a significantly higher mortality risk (hazard ratio [HR], 1.34) upon regression analysis. Patients treated with Flu-Cy-2GyTBI had the highest 4-year adjusted OS (67%), followed by those in the Flu-Cy cohort (63%), the Flu-Bu cohort (58%), and the Flu-Mel140 cohort (49%). No significant differences in OS were seen between Flu-Bu, Flu-Cy-2GyTBI, and the Flu-Cy patients. Treatment with Flu-Mel140 was associated with a higher non-relapse mortality compared with Flu-Bu (HR, 1.78). The 4-year adjusted cumulative incidence of non-relapse mortality was 26% in the Flu-Mel140 cohort, followed by 17% in both the Flu-Cy-2GyTBI and Flu-Cy groups, and 16% in the Flu-Bu cohort.

Patients in the Flu-Cy cohort had the highest adjusted cumulative incidence of relapse or progression at 4 years (50%), followed by those in the Flu-Bu cohort (47%), the Flu-Mel140 cohort (37%), and the Flu-Cy-2GyTBI cohort (33%). Upon regression analysis, however, differences between the Flu-Mel140 and Flu-Bu cohorts were not significantly different (HR, 0.79).

Adjusted 4-year progression-free survival (PFS) was highest with Flu-Cy-2GyTBI treatment (51%), followed by Flu-Mel140 (39%), Flu-Bu(38%),andFlu-Cy(35%).Comparedwith Flu-Bu, however, PFS was not significantly improved with Flu-Mel140 (HR, 1.03), Flu-CY-2GyTBI (HR, 0.70), or Flu-Cy (HR, 1.07) upon adjustment.