ISSUE 28 · DECEMBER 2021

APPE TRAILS

Official Newsletter for P3 and P4 Students at Manchester University College of Pharmacy, Natural and Health Sciences

Online Veterinary Pharmacy Course

BY THE OFFICE OF EXPERIENTIAL EDUCATION

The National Association of Boards of Pharmacy has recognized the need for pharmacists to possess the competence to care for veterinary patients. NABP passed a resolution encouraging the availability of veterinary pharmacology education. The Online Course in Veterinary Pharmacy for pharmacy students continues to address the need for veterinary pharmacy curricular offerings by using distance education technology.

Students are welcome to take the 2-credit hour course on an individual basis and transfer the elective credit back to their home school. The course is offered every spring, summer and fall semester.

University of Florida College of Pharmacy welcomes registrations for the spring 2022 course offering. The course starts January 5th, 2022, and ends in late April. For information on course objectives, dates, tuition, or registration instructions click here. To register for the course, you will need to apply for admission to UF as a non-degree student. (Click on the Apply button on the blue menu bar to begin the application. Please read carefully and follow exactly the Step #2 Non-degree application instructions for Veterinary Pharmacy so that you apply for the correct special program).

For questions on this one-of-a-kind course contact Elaine Blythe, PharmD.
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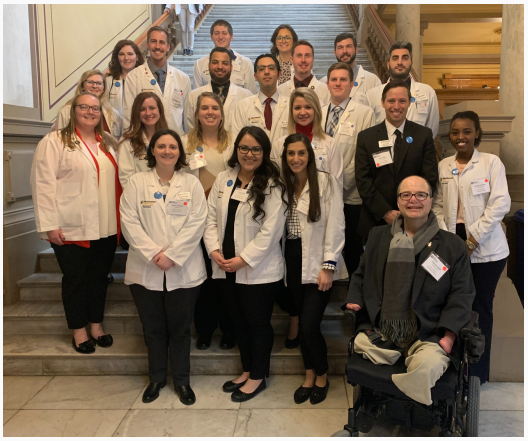

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Wellness Survey

BY MICHELLE KIBIGER, DIRECTOR OF ASSESSMENT

The Pharmacy Programs' Strategic Plan Initiative 1: People; addresses the wellness of our students, faculty, and staff within the programs as well as the improved wellness of the surrounding community.

An anonymous Wellness Survey is being administered to all students, faculty, and staff in the pharmacy programs in order to:
1) identify the baseline wellness of the programs,
2) guide future wellness programming, and
3) assess if diverse groups are experiencing similar levels of wellness.

The survey takes approximately 15 minutes to complete. An optional action plan (available in CE section, Class of page) may be completed to develop a personal wellness goal based on your survey results. You may choose to upload the completed action plan for 1 CE credit in self-awareness. Thank you for completing the survey. We appreciate your time and input.

Michelle Kibiger, Director of Assessment (mjcordova-kibiger@manchester.edu)

APPE Spotlight

BY THE OFFICE OF ADMISSIONS AND ENROLLMENT MANAGEMENT

Email our admissions team to be featured on social media! Include 1-3 sentences about your current rotation site and a picture of yourself! Email healthsciences@manchester.edu.

Pembrolizumab indication for early triple-negative breast cancer: FDA Approval

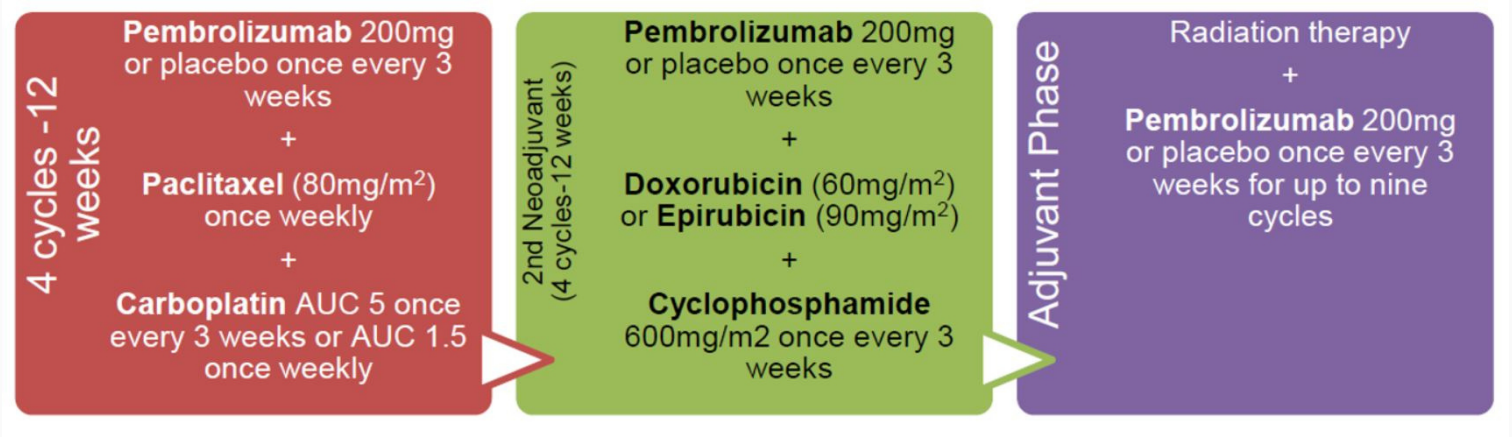
BY MARK BOTROS, PHARMD CANDIDATE 2022

Despite advances in immunotherapy, HER-2 and hormone receptor-negative breast cancers (commonly referred to as triple-negative breast cancers [TNBC]) account for about 10-15% of all breast cancers and remain among the most challenging types of cancer to treat. Due to the lack of specific tumor targets, prior national comprehensive cancer network (NCCN) guidelines have recommended using a host of nonspecific chemotherapy agents for curative and palliative intents alike with poor treatment outcomes. The lack of alternatives has encouraged authors to investigate the benefit of using pembrolizumab (Keytruda®), a programmed death ligand-1 (PD-L1) antagonist in early triple-negative breast cancer regardless of PDL-1 status.

Cancerous tumors commonly target PDL-1, found on T-cells, to inhibit immune system detection of uncontrolled growth. Agents such as Pembrolizumab (Keytruda), an anti-PD-1 humanized monoclonal antibody, bind and inhibit programmed death receptors on T-cells. This binding to PD-L1 receptors on T-cells reverses the tumor-modulated immune regulation inhibition and allows for a regular anti-tumor response by the immune system. After the publication of this study and thorough FDA review, pembrolizumab received an indication for early TNBC along with chemotherapy as neoadjuvant and adjuvant treatments, and shortly after was adopted by oncology treatment guidelines such as the NCCN.

METHODS

The primary study (KEYNOTE-522 NCT03036488) fueling this approval was aimed at comparing the safety and efficacy of neoadjuvant and adjuvant pembrolizumab against placebo, where both groups received standard chemotherapy treatment in early stages of TNBC. This randomized, double-blind phase III trial recruited 1174 patients from 21 countries with confirmed previously untreated diagnosis of non-metastatic TNBC with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The regimen used is described below:



Primary endpoints looked at achieving pathological complete response (disappearance of invasive cancer and negative nodes) (pCR) at time of surgery and event-free survival. Event-free survival in this study included progression of disease, local or distant recurrence, and a second primary malignancy or death from any cause from time of randomization.

Pembrolizumab indication for early triple-negative breast cancer: FDA Approval Continued...

BY. MARK BOTROS, PHARMD CANDIDATE 2022

RESULTS

The interim analysis showed a 13.6% increase in achieving pCR with the pembrolizumab group (64.8% vs. 51.2% pembrolizumab-chemotherapy group vs. placebo-chemotherapy, respectively, 95% CI, 5.4 to 21.8; P<0.001). Pathological complete response, a unique primary endpoint, has been shown to correlate with improved overall survival. Additionally, an increase in pCR to 64.8% from the standard 40-50% observed in previous studies of platinum-based chemotherapy with taxanes in TNBC is a significant increase, further highlighting the efficacy benefit of pembrolizumab. As for the event-free survival endpoint, 11.8% in the placebo group compared to 7.4% in the treatment group had a qualifying event to interrupt event-free survival.

Safety analysis showed comparable profiles for both placebo and pembrolizumab groups in the neoadjuvant and adjuvant phases. In the adjuvant phase, 48.1% of patients in the pembrolizumab-chemotherapy group and 43% of the placebo-chemotherapy group experienced treatment-related adverse effects. While in the neoadjuvant phase, grade 3 or higher treatment-related adverse events occurred in 76.8% of the pembrolizumab-chemotherapy group and 72.2% of the placebo-chemotherapy group.

Improvement in treatment coupled with the observed comparable safety profile of the pembrolizumab treatment group in both neoadjuvant and adjuvant stages of treatment prompted the indication approval on July 26, 2021. The approved pembrolizumab dosing schedule, similar to the study design, is 200 mg every three weeks or 400 mg every six weeks as an intravenous infusion over 30 minutes. Administered with chemotherapy, pembrolizumab treatment is indicated for 24 weeks in the neoadjuvant treatment phase followed by a duration of up to 27 weeks without chemotherapy in the adjuvant treatment phase.

An interesting aspect of this study design is the recruitment of PD-L1 negative cancer patients. Despite our mechanistic understanding of pembrolizumab, PD-L1 status was not an inclusion/exclusion criteria. In fact, 16-17% of the total sample population was PD-L1 negative at baseline. PD-L1 status helps identify the genomic nature of the tumor and thereby appropriate target treatment. PD-L1 negative status indicates that this particular tumor doesn't express PD-1 ligands and thereby shouldn't be responsive to a PD-L1 antagonist such as pembrolizumab.

Interestingly, the difference in complete pathological response is similar in both groups when results are stratified by PD-L1 status. However, PD-L1 status representation is not balanced between groups, with 81-83% of both arms as PD-L1 positive. Despite the authors' attempts to design the study allowing for broader generalizability of the data to early-stage TNBC patients regardless of PD-L1 status, it is questionable whether the results can truly apply to PD-L1 negative tumors considering the smaller sample size of this group. Aside from this design component, the overall study design is a major strength comparing intervention to placebo in a randomized controlled trial. Additionally, the ability to compare safety between placebo-chemotherapy and pembrolizumab-chemotherapy groups is a strength particularly when both arms are similar in terms of treatment regimen and are comprised of many toxic chemotherapy drugs with abysmal side effect profiles. By using this study design allowing for direct comparisons, we can evaluate the safety of pembrolizumab and its impact on chemotherapy-related adverse effects.

Pembrolizumab indication for early triple-negative breast cancer: FDA Approval Continued...

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CONCLUSIONS

KEYNOTE-522 trial showed a clinically and statistically significant increase in pCR when pembrolizumab is added to neoadjuvant chemotherapy with additional survival benefits in the adjuvant phase. Aggressive types of cancer such as TNBC are incredibly challenging to treat. Scarce treatment options coupled with lower success rates have been a salient concern for the oncology community. This study and approval provide much hope and a potential renewed confidence in the treatment efficacy of early-stage TNBC in the form of targeted immune therapy.

REFERENCES

· Food and Drug Administration. FDA approves pembrolizumab for high-risk early-stage triple-negative breast cancer. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-high-risk-early-stage-triple-negative-breast-cancer. Last revised on Jul 27, 2021.

· American Cancer Society. Triple-Negative Breast Cancer. https://www.cancer.org/cancer/breast-cancer/about/types-of-breast-cancer/triple-negative.html. Last revised on Jan 27, 2021.

· Ismail-Khan R, Bui MM (2010) A review of triple-negative breast cancer. Cancer Control 17(3):173176

· Cetin B, Gumusay O. Pembrolizumab for Early Triple-Negative Breast Cancer. N Engl J Med. 2020;382(26):e108. doi:10.1056/NEJMc2006684

· Sasanpour P, Sandoughdaran S, Mosavi-Jarrahi A, Malekzadeh M. Predictors of Pathological Complete Response to Neoadjuvant Chemotherapy in Iranian Breast Cancer Patients. Asian Pac J Cancer Prev. 2018;19(9):2423-2427. Published 2018 Sep 26.

· Pandy JGP, Balolong-Garcia JC, Cruz-Ordinario MVB, Que FVF. Triple negative breast cancer and platinum-based systemic treatment: a meta-analysis and systematic review. BMC Cancer. 2019;19(1):1065. Published 2019 Nov 8.

· Chen Y, Guan Y, Wang J, et al. Platinum-based chemotherapy in advanced triple-negative breast cancer: A multicenter real-world study in China. Int J Cancer. 2020;147(12):3490-3499.

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