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## 627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

### Small-Dose Trimethoprim-Sulfamethoxazole Prevents Pneumocystis Jiroveci Pneumonia in B-Cell Lymphoma Patients Receiving Chemotherapy: Analysis of a Randomized Controlled Clinical Trial

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B-cell lymphoma is the most common non-Hodgkin lymphoma and is usually treated with the R-CHOP regimen. However, some patients might develop interstitial pneumonitis (IP), which has led to death in some patients. With advances in detection techniques, infections are now considered to be an important etiologic factor in IP, particularly the common opportunistic causative agent Pneumocystis jiroveci. A retrospective cohort analysis at our center has tentatively elucidated that TMP-SMX can achieve effective IP prevention. There are no prospective studies to confirm the preventive effect of TMP-SMX and its mechanism.

A single-arm, single-center, randomized controlled clinical trial of TMP-SMX for the prevention of interstitial pneumonitis was conducted at our center. Prophylactic treatment with TMP-SMX in patients in the treatment group was turned on immediately after starting chemotherapy and continued until one month after the end of chemotherapy. The dose of prophylactic treatment was 0.16 g of TMP/0.8 g of SMX once daily.

From April 26, 2022, to July 25, 2023, a total of 198 patients with the diagnosis of B-cell lymphoma met the criteria for enrollment and were randomly assigned to the control and treatment groups. Eleven were lost to follow-up before completing 4 courses of chemotherapy, 19 did not complete 4 courses of chemotherapy as of July 25, 2023, and 3 were excluded from the evaluation when they were switched to chemotherapy with other regimens not based on R-CHOP because of poor efficacy after 1 course of chemotherapy, among other reasons. 80 patients in the treatment group and 85 in the control group were finally included in the assessment (Figure 1, Figure 2).

There were no statistical differences between patients in the control and treatment group in terms of baseline clinical characteristics such as gender, age, smoking history, lung disease, type of pathology, Ann Arbor stage, LDH level, ECOG score, IPI score, chemotherapy regimen, and group B symptoms.

Observation of the primary outcome events in this study showed a significant reduction in the incidence of IP (5.0% vs 47.1%, $P<0.001$) and PJP (0.0% vs 28.2%, $P<0.001$) in the patients in the treatment group (Figure 2). IP occurred in 4 (5.0%) in the treatment group, and retrospective patient characteristics revealed that all were COVID-19, in addition to no patients developing IP. Forty (47.1%) in the control group developed IP, 16 were COVID-19, and 24 patients had a complete bronchoscopy with alveolar lavage sent for NGS, all of which revealed PJs or concomitant other pathogens. As of July 25, 2023, 1 patient discontinued TMP-SMX because of the development of renal insufficiency. There have been no deaths due to PJP in patients enrolled in this clinical trial at our center. The results of the subgroup analyses showed that TMP-SMX prophylaxis in any subgroup significantly reduced the risk of IP and there was no interaction.

Of the 44 patients who developed IP, 24 underwent bronchoscopy, and PJ was detected by alveolar lavage NGS in all of them, and other pathogens such as Streptococcus pneumoniae, human herpesvirus, Catamoeba, and Candida albicans were detected in some patients. The median number of chemotherapy cycles in which IP occurred was 4 (Figure 1).
In the control group, between patients who developed IP and those who did not, there were statistically significant differences in LDH levels (IP 237.0 (194.5, 398.0) vs Non-IP 198.0 (161.0, 278.0), P=0.032), R-CDOP chemotherapy regimen (IP 67.5% vs Non-IP 42.2%, P=0.004) difference, and the rest of the factors did not differ between the two groups. Binary logistic regression analysis of risk factors for the development of IP in the control group showed that patients on the R-CDOP chemotherapy regimen had a significantly increased risk of IP (OR=2.72, 95% CI 1.09-6.80, P=0.033), whereas there was no significant difference between age and LDH.
As the chemotherapy cycle progressed, the patients' $CD4^+$ T-cell counts gradually decreased, with the same trend in the control group as in the treatment group.
In patients receiving chemotherapy with R-CHOP/R-CDOP-based regimens, the majority of IP that occurs is PJP and prevention with TMP-SMX is safe and effective. Patients treated with PLD have a higher risk of IP occurrence.

**Disclosures** No relevant conflicts of interest to declare.

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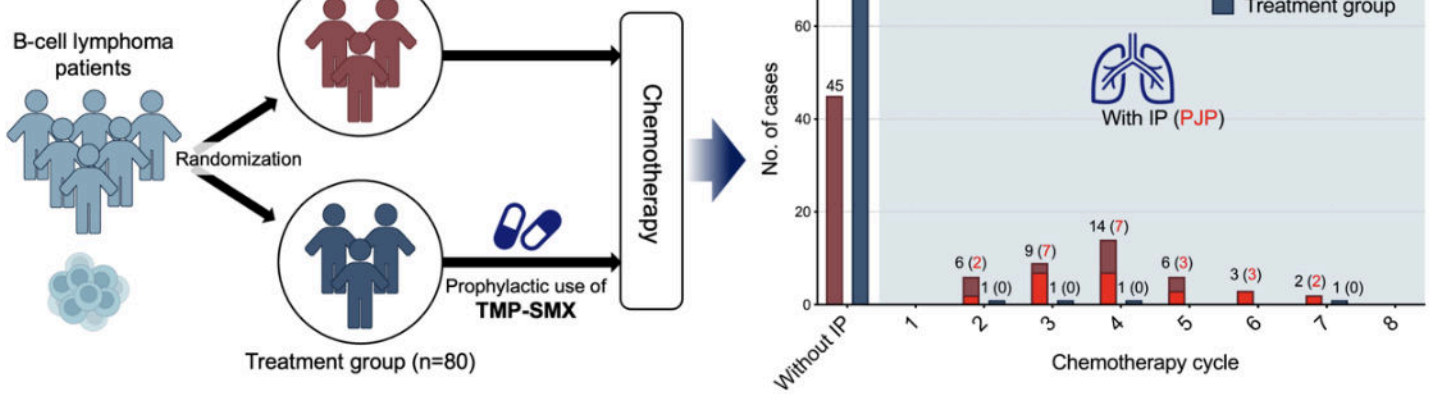


Figure 1 Research Summary Chart

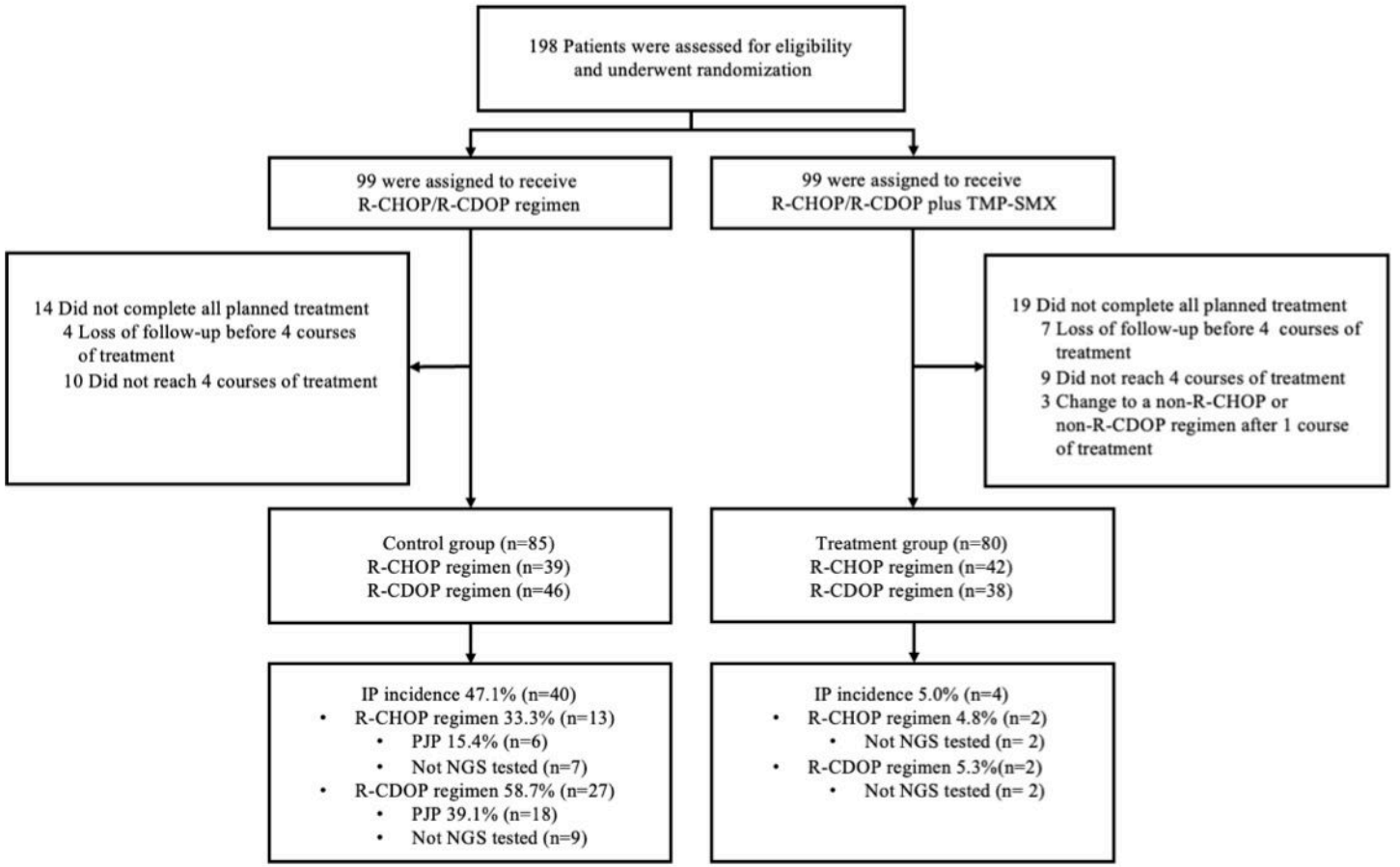


Figure 2 Enrollment, Randomization, and Outcome