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Fluorodeoxyglucose-positron emission tomography/computed tomography-based chemotherapy dosage adjustment in seminoma: The GETUG SEMITEP trial

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SUMMARY

In men with metastatic seminoma, negative fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) imaging indicates the absence of live seminoma cells[1] in the residual disease following chemotherapy. In this trial,[2] an interim FDG-PET/CT scan was used to determine whether men with favorable prognosis metastatic seminoma may be treated with two cycles of etoposide-cisplatin (EP) followed by only one cycle of carboplatin (CARBO), thus reducing the burden of treatment and toxicities.

The GETUG SEMITEP is a phase 2, nonrandomized, multicenter study of men withfavorable prognosis metastatic seminoma (stages IIB and III). Between 2013 and 2017, 102 patients were recruited. All patients with baseline-positive FDG-PET/CT received two EP cycles. Patients had a second FDG-PET/CT scan 17–20 days following their second EP cycle to assess their progress. Four cycles of EP were given to patients with persistently positive FDG-PET/CT, whereas only one cycle of CARBO was given to others who achieved FDG-PET/CT-negative status at interim analysis. The primary outcome was proportion of persons who underwent de-escalating treatment following a negative interim FDG-PET/CT scan. The secondary objectives were progression-free survival (PFS) and overall survival (OS).

Three individuals were found to be ineligible for evaluation, resulting in the therapy of 99 people. FDG-PET/CT was available in 98 participants following the first two EP cycles as one of the patients died due to toxicity after the second EP cycle. It was shown that 72.4% of participants (71 patients) achieved negative FDG-PET/CT results at the interim FDG-PET/CT. Four of such 71 participants still wanted normal treatment (EP four cycles), and 67 participants (68.4%; 95% CI: 58.2–77.4) received one cycle of carboplatin following two cycles of EP, satisfying their primary outcome.

Following two EP cycles, 27 participants (27.6%; 95% CI: 19.0-37.5) still had a positive FDG-PET/CT; so a total of 31 patients received two more EP cycles. Nine patients had relapsed after an average follow-up of 39.4 months (three patients in EP and six in CARBO). The 3-year PFS rate in the EP group was 90.0% (95% confidence interval [CI] 74.4–96.5) and 90.2% (95% CI: 80.2–95.5) in the CARBO group. Seventeen of 31 patients who underwent four cycles of EP suffered neurological toxicities, whereas just four of 67 carboplatin patients did. Fourteen and 15 patients in the EP and carboplatin groups had ototoxicity, respectively. In the EP group, peripheral neuropathy and ototoxicity were more common ($P < 0.0001$ and $P = 0.02$, respectively). There were no reports of cardiac toxicity. There was no substantial difference in nephrotoxicity between the two groups ($P = 0.6$).

COMMENTS

Men treated for seminoma with residual lymph nodeal masses >3 cm after chemotherapy should undergo FDG-PET, and for patients with FDG-PET avid lesion, salvage therapy is necessary.[3]

In another trial,[4] individuals with advanced-stage seminoma were given either BEP or EP. FDG-PET/CT was performed at the start of the study, after two rounds (PET/CT2), and after treatment. The 5-year relapse-free survival rate for PET/CT2-positive patients was 75% (95% CI, 60–95) and 97.8% for PET/CT2-negative patients (93.7–100, $P = 0.001$). In univariate analysis, PET/CT2 was shown to be substantially linked with relapse-free survival ($P = 0.02$). The authors concluded that no FDG uptake after two cycles of standard chemotherapy is prognostic in advanced seminoma and could be considered for chemotherapy de-escalation.

De-escalation treatments are feasible and had an initial favorable toxicity profile, according to another study with stage II A/B seminoma (de novo or relapsed), which used one cycle of carboplatin followed by radiation therapy to the involved node with 30 Gy in stage IIA and 36 Gy in stage IIB.[5]

GETUG SEMITEP trial shows de-escalation of chemotherapy based on early FDG-PET/CT in metastatic seminoma is possible. This reduces neuropathy, ototoxicity, and other related side effects with equivalent early PFS and OS. To assure that de-escalation treatment does not cause late recurrence, the trial's median follow-up duration should be prolonged to establish long-term toxicity, PFS, and OS.

Some centers are adopting therapy de-escalation to reduce side effects, treatment time, quality of life, and expenses while preserving cure rates. However, due to a dearth of randomized control trials, de-escalation treatments are still to be acknowledged as standard of care and further studies are needed to confirm the results of the SEMITEP trial.

REFERENCES

1. Bachner M, Loriot Y, Gross-Goupil M, Zucali PA, Horwich A, Germa-Lluch JR, *et al.* 2-^{18}fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: A retrospective validation of the SEMPET trial. Ann Oncol 2012;23:59-64.
2. Loriot Y, Texier M, Culine S, Fléchon A, Thiery-Vuillemin A, Gravis G, *et al.* The GETUG SEMITEP trial: De-escalating chemotherapy in good-prognosis seminoma based on fluorodeoxyglucose positron emission tomography/computed tomography. Eur Urol 2022;82:172-9.
3. De Santis M, Becherer A, Bokemeyer C, Stoiber F, Oechsle K, Sellner F, *et al.* 2-18fluoro-deoxy-D-glucose positron emission tomography is a reliable predictor for viable tumor in postchemotherapy seminoma: An update of the prospective multicentric SEMPET trial. J Clin Oncol 2004;22:1034-9.
4. Raggi D, Bandini M, Giannatempo P, Farè E, Marandino L, Colecchia M, *et al.* Prognostic role of early interim fluorodeoxyglucose positron emission tomography in patients with advanced seminoma undergoing standard treatment. Clin Genitourin Cancer 2021;19:237-45.e2.
5. Papachristofilou A, Bedke J, Hayoz S, Fischer N, Schiel X, Schratzenstaller U, *et al.* Treatment compliance and early toxicity in SAKK 01/10: Single-dose carboplatin and involved-node radiotherapy for treatment of stage IIA/B seminoma. Journal of Clinical Oncology 2020; 38:6_suppl, 405-405.

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