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Reduced radiotherapy by combining chemotherapy with intrathecal administration of methotrexate for pediatric patients with intracranial germ cell tumor

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Abstract

Background: Treatment of intracranial germ cell tumors (GCTs) involves radiation therapy to the whole ventricle or the whole neuroaxis, but late sequelae are a concern. Therefore, an alternative modality is needed to reduce the overreliance on radiation therapy. Intrathecal methotrexate (IT-MTX) was examined as a partial alternative to radiotherapy. Procedure: Low-risk (LR) patients (germinoma) were treated with four cycles of cisplatin, etoposide, and IT-MTX, while intermediate-risk (IR) (human chorionic gonadotropin [HCG]-producing germinoma) and high-risk (HR) (non-germinomatous GCT) patients were treated with five cycles of cisplatin, etoposide, cyclophosphamide, and IT-MTX. Local irradiation of 24 Gy was performed for the LR and IR patients, while irradiation with 51.2 Gy was performed for the HR cases. For patients with multifocal diseases and/or tumors extending to the 3rd ventricle, whole ventricle irradiation was performed. Results: A total of 57 patients were enrolled, of which three withdrew consent. Thus, 54 patients were included in the outcome analysis. The 5-year progression-free survival and overall survival were 92.0% (standard error 4.4%) and 100%, respectively, for 28 LR and 10 IR patients (median follow-up: 63 months), and 86.7% (8.8%) and 93.3% (6.4%) (median follow-up: 67 months), respectively, for 16 HR patients. The major toxicity was hematological, and most patients experienced grade 4. Conclusion: The toxicity of chemotherapy containing IT-MTX was limited, and the results suggested that this regimen could reduce the need for radiotherapy.

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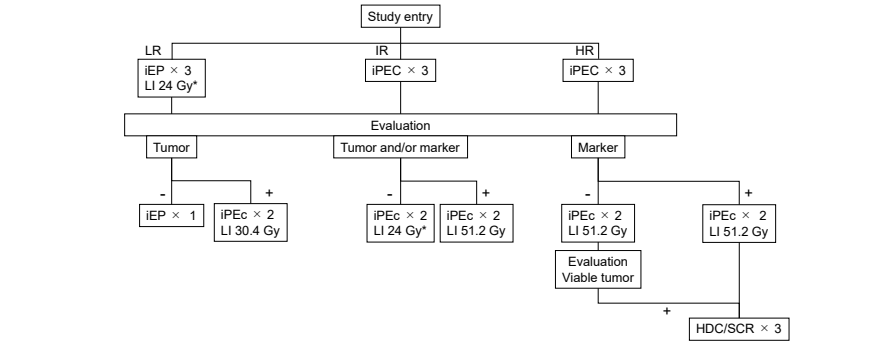
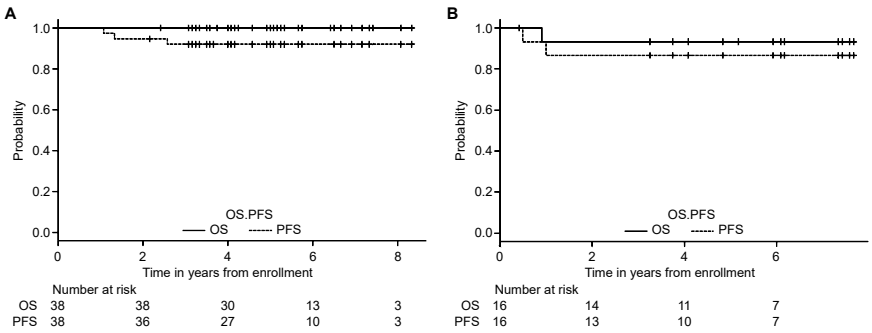


iEP regimen	iPEC regimen	iPEc regimen	HDC
Etoposide 100 mg/m^2/day days 1-5	Etoposide 100 mg/m^2/day days 1-5	Etoposide 100 mg/m^2/day days 1-5	Etoposide 400 mg/m^2/day days 1-3
Cisplatin 90 mg/m^2/day day 1	Cisplatin 90 mg/m^2/day day 2	Cisplatin 90 mg/m^2/day day 2	Carboplatin AUC 7/day days 1-3
IT-methotrexate 12 mg/dose day 1	Cyclophosphamide 1 g/m^2/day day 1, 3, 5	Cyclophosphamide 1 g/m^2/day day 1	
IT-dexamethasone 8 mg/dose day 1	IT-methotrexate 12 mg/dose day 1	IT-methotrexate 12 mg/dose day 1	
	IT-dexamethasone 8 mg/dose day 1	IT-dexamethasone 8 mg/dose day 1	
	Mesna 200 mg/m^2/dose (3 doses/day) days 1, 3, 5	Mesna 200 mg/m^2/dose (3 doses/day) day 1	

18 Gy CSI to patients with spinal dissemination.

*: WVI to patients with multicentric tumors or tumors extending to the third ventricular instead of LI.



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