

CSF Diversion Facilitates Further Systemic Therapy in Leptomeningeal Hydrocephalus

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Research Article

Keywords:

Posted Date: September 4th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10805344/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Leptomeningeal disease (LMD) is a complication of metastatic cancer frequently accompanied by symptomatic hydrocephalus. CSF shunting has traditionally been considered palliative, providing symptomatic relief. In the era of CNS-penetrating systemic therapies, factors associated with post-shunt outcomes remain incompletely characterized. We evaluated clinical outcomes following CSF shunting for LMD-associated hydrocephalus and identified predictors of oncologic benefit.

Methods

We performed a retrospective cohort study of 51 consecutive patients with LMD-associated hydrocephalus who underwent CSF shunting. Clinical, radiographic, molecular, treatment, and outcome data were collected. The primary endpoint was symptomatic improvement and receipt of post-shunt oncologic therapy. Secondary endpoints included overall survival (OS), estimated using the Kaplan-Meier method and Cox regression.

Results

We included 51 patients with a median pre-shunt KPS of 60. Brain metastases were present in 60.8% and breast cancer (43.1%) was the most common. Clinical improvement occurred in 40 of 49 evaluable patients (81.6%), with the greatest improvement in nausea/vomiting (62.5%) and headache (58.1%). Following shunting, 41 patients (80.4%) received additional oncologic therapy, including 20 (39.2%) who received CNS-penetrating therapy. Median OS was 70 days (95% CI, 54–156). CNS-penetrating therapy was associated with longer survival (193 vs. 49 days; log-rank $p = 0.0001$). In multivariable analysis, cranial nerve involvement was independently associated with worse survival (HR 4.25, 95% CI 1.75–10.32; $p = 0.001$), whereas post-shunt therapy (HR 0.078, 95% CI 0.022–0.282; $p < 0.001$) and CNS-penetrating therapy (HR 0.266, 95% CI 0.116–0.612; $p = 0.002$) were associated with improved survival. Brain metastases were also associated with inferior survival (HR 2.86, 95% CI 1.10–7.46; $p = 0.032$).

Conclusions

CSF shunting provides meaningful symptomatic benefit in patients with LMD-associated hydrocephalus and enables subsequent treatment. Receipt of CNS-penetrating therapy was associated with prolonged survival, whereas cranial nerve involvement and brain metastases identified patients with poorer prognosis. These findings support integrating CSF diversion with contemporary CNS-active therapies in selected patients with LMD.

Introduction

Leptomeningeal disease (LMD) is an end-stage complication of metastatic cancer characterized by malignant cell dissemination throughout the leptomeninges and cerebrospinal fluid (CSF)[1], [2]. It occurs in approximately 5–8% of patients with solid tumors, most commonly breast cancer, lung cancer, and melanoma[3], [4]. Its incidence is increasing as advances in systemic therapy prolong survival in metastatic cancer[5], [6]. Nevertheless, prognosis remains poor, with median survival ranging from several weeks to a few months[1], [4].

LMD has heterogeneous manifestations reflecting multifocal neuraxis involvement, including headache, cranial neuropathies, radiculopathies, gait dysfunction, and cognitive impairment[2], [7]. Hydrocephalus is a clinically significant complication affecting up to half of patients, primarily due to impaired CSF resorption from leptomeningeal tumor infiltration[1], [8], [9].

Ventriculoperitoneal shunting is the most widely used treatment for LMD-associated hydrocephalus and provides rapid symptomatic relief in most patients[10], [11]. Systematic reviews and meta-analyses report improvement rates approaching 80%; however, shunting remains palliative and may not be offered in some clinical scenarios[1], [2]. Beyond palliation, shunting may enable further cancer-directed therapy, including systemic treatments with CNS activity. As CNS-penetrating targeted therapies and immunotherapies assume a greater role in LMD management, understanding the relationship between CSF diversion and subsequent treatment has become increasingly important[10], [12], [13].

Few studies have systematically evaluated prognostic factors while accounting for baseline performance status, disease burden, and contemporary CNS-active therapies. We therefore evaluated 51 patients who underwent CSF shunting for LMD-associated hydrocephalus at a single institution. We characterized symptomatic outcomes and post-shunt treatment patterns and identified clinical, radiographic, and treatment-related predictors of overall survival, emphasizing the impact of CNS-penetrating therapies.

Methods

Study Design and Patient Population

We conducted a retrospective, single-center cohort study of patients with leptomeningeal disease (LMD) who underwent cerebrospinal fluid (CSF) shunting for symptomatic hydrocephalus. Consecutive adults were identified through institutional databases and electronic medical record review. LMD was diagnosed by magnetic resonance imaging (MRI), CSF cytology, or both. Patients with incomplete survival data were excluded from survival analyses. Institutional review board and local ethics committee approval were obtained; patient consent was waived due to the retrospective design.

Data Collection and Clinical Variables

Demographic, clinical, radiographic, molecular, treatment, and outcome data were collected by chart review. Variables included age, sex, primary tumor type, Karnofsky Performance Status (KPS), Eastern Cooperative Oncology Group (ECOG) performance status, and pre-shunt neurologic symptoms, including headache, nausea/vomiting, gait disturbance, cognitive decline, visual symptoms, and urinary incontinence. Radiographic and CSF variables included cytology; MRI LMD pattern (diffuse or nodular); spinal and cranial nerve involvement; anatomic LMD location; and the presence, number, location, and volume of brain metastases. Brain metastases were classified as absent, solitary, or multiple (≥ 2 lesions). Tumor volume, when available, was analyzed continuously and by cohort median.

Prior CNS-Directed Therapy

Prior CNS-directed treatments included tumor resection, whole-brain radiotherapy (WBRT), stereotactic radiosurgery (SRS), and intrathecal chemotherapy. Patients were classified as CNS treatment-naïve or previously treated before shunting.

Molecular Characterization

Tumors were categorized as breast cancer, lung cancer, melanoma, or other malignancies. Available molecular data included HER2 status and molecular subtype in breast cancer; EGFR, ALK, ROS1, KRAS, and PD-L1 status in lung cancer; and BRAF and NRAS status in melanoma. Tumors harboring targetable genomic alterations were classified as actionable.

CSF Shunting and Clinical Outcomes

All patients underwent CSF diversion for symptomatic hydrocephalus. Shunt-related variables included shunt and valve type, infection, malfunction, revision, and peritoneal tumor seeding. Clinical response was retrospectively assessed from postoperative documentation, with symptoms classified as improved, unchanged, worsened, or unavailable. Symptom-specific analyses included headache, nausea/vomiting, gait disturbance, cognitive decline, visual symptoms, and urinary incontinence. Overall response was dichotomized as responder or non-responder based on documented postoperative improvement. Receipt of subsequent oncologic therapy was also recorded.

Post-Shunt Oncologic Therapy

Post-shunt treatments were categorized as systemic chemotherapy, targeted therapy, immune checkpoint inhibitor therapy, intrathecal chemotherapy, radiation therapy, or surgery. Any post-shunt therapy was defined as receipt of at least one treatment modality, whereas combination therapy required multiple modalities. Therapies with documented activity against leptomeningeal or intracranial metastatic disease were classified as CNS-penetrating. These included osimertinib, neratinib,

abemaciclib, capecitabine, trastuzumab deruxtecan, olaparib, methotrexate, and cytarabine (Supplementary Table S3).

Study Endpoints

Primary endpoints were overall clinical response, symptom-specific improvement, and receipt of post-shunt oncologic therapy. Secondary endpoints included overall survival (OS), defined as the interval from shunt placement to death from any cause, and clinical, radiographic, molecular, and treatment-related predictors of survival and treatment response. Clinical improvement was defined as documented symptom resolution, reduced severity or use of symptom-directed medications, or functional improvement attributable to the symptom domain. Formal Response Assessment in Neuro-Oncology-Leptomeningeal Metastases (RANO-LM) criteria could not be applied retrospectively.

Statistical Analysis

Categorical variables were summarized as frequencies and percentages and continuous variables as medians with interquartile ranges (IQRs) or means with standard deviations, as appropriate. Fisher's exact tests compared categorical variables. OS was estimated using the Kaplan-Meier method and compared by log-rank testing. Univariable Cox proportional hazards regression identified factors associated with survival. Statistically significant or clinically relevant variables were incorporated into multivariable Cox models. Because baseline functional status is an established prognostic factor in LMD, KPS was included a priori in the primary multivariable model regardless of statistical significance. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. Model discrimination was assessed using the concordance index (C-index), and proportional hazards assumptions using Schoenfeld residuals. All tests were two-sided, with $p < 0.05$ considered statistically significant. Analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient Characteristics

The study included 51 patients with leptomeningeal disease (LMD) and symptomatic hydrocephalus who underwent cerebrospinal fluid (CSF) shunting (Table 1). The cohort comprised 36 women (70.6%) and 15 men (29.4%). Primary malignancies included breast cancer in 22 patients (43.1%), lung cancer in 10 (19.6%), melanoma in 4 (7.8%), and other malignancies in 15 (29.4%). Baseline performance status was generally poor, with a median Karnofsky Performance Status (KPS) of 60 and most patients having an Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2 .

Table 1
Baseline Demographic, Clinical, and Radiographic
Characteristics of Patients Undergoing CSF Shunting for
Leptomeningeal Disease

Characteristic	N = 51
Sex	
Female	36 (70.6%)
Male	15 (29.4%)
Primary Cancer Group	
Breast	22 (43.1%)
Lung	10 (19.6%)
Melanoma	4 (7.8%)
Other	15 (29.4%)
Pre-shunt Performance Status	
KPS, median (IQR)	60 (50–70)
ECOG, median (IQR)	2 (2–3)
CSF Cytology	
Positive	38 (74.5%)
Negative	8 (15.7%)
Unknown/NA	5 (9.8%)
MRI LMD Pattern	
Diffuse	30 (58.8%)
Nodular	17 (33.3%)
Unknown/NA	4 (7.8%)
Disease Characteristics	
Spine involvement	11 (21.6%)
Cranial nerve involvement	14 (27.5%)
Brain metastases present	33 (60.8%)
No brain metastases	18 (39.2%)
Single brain metastasis	9 (17.6%)

Characteristic	N = 51
Sex	
Multiple brain metastases (≥ 2)	24 (47.1%)
Intracranial tumor volume, cm ³ , median	4.56
Tumor volume data available	22 (43.1%)
Pre-shunt Symptoms	
Headache	36 (70.6%)
Nausea/Vomiting	24 (47.1%)
Gait disturbance	33 (64.7%)
Cognitive decline	34 (66.7%)
Vision symptoms	22 (43.1%)
Urinary incontinence	5 (9.8%)
Prior CNS-Directed Treatments	
CNS treatment naïve	24 (47.1%)
Prior tumor resection	11 (21.6%)
Prior whole-brain radiation therapy	9 (17.6%)
Prior stereotactic radiosurgery	13 (25.5%)
Prior intrathecal chemotherapy	4 (7.8%)
Prior external ventricular drain (EVD)	23 (45.1%)

LMD was diagnosed by MRI and lumbar puncture in 48 patients (94.1%) and MRI alone in 3 (5.9%). CSF cytology was positive in 38 patients (74.5%), negative in 8 (15.7%), and unavailable or indeterminate in 5 (9.8%). LMD was diffuse in 30 patients (58.8%) and nodular in 17 (33.3%). Spinal and cranial nerve involvement occurred in 11 (21.6%) and 14 patients (27.5%), respectively. Brain metastases occurred in 33 patients (65%): 9 (17.6%) had a solitary metastasis and 24 (47.1%) had multiple lesions. Tumor volume was available for 22 patients, with a median of 4.56 cm³ (interquartile range [IQR], 1.11–10.05 cm³). Baseline symptoms included headache in 70.6%, gait disturbance in 64.7%, cognitive decline in 66.7%, nausea/vomiting in 47.1%, visual symptoms in 43.1%, and urinary incontinence in 9.8% (Table 1).

Timing of Disease Course and Post-Shunt Therapy

LMD developed a median of 589 days (IQR, 219–1361 days) after primary cancer diagnosis (Table 2). CSF shunting was performed a median of 8 days (IQR, 3.5–31.5 days) after LMD diagnosis. Among

patients who received post-shunt therapy and had available timing data (n = 21), treatment began a median of 6 days (IQR, 0–13 days) after shunting.

Table 2
Timing of Disease Course and Post-Shunt Therapy

Interval	Median	IQR
Primary cancer diagnosis → LMD diagnosis	589 days (19.4 months)	219–1361 days
LMD diagnosis → shunt placement	8 days	3.5–31.5 days
Shunt placement → first post-shunt therapy	6 days	0–13 days

Clinical Outcomes Following CSF Shunting

Among evaluable patients, improvement occurred in headache (58.1%), nausea/vomiting (62.5%), gait disturbance (47.1%), cognitive decline (33.3%), visual symptoms (25.0%), and urinary incontinence (50.0%). Symptoms associated with elevated intracranial pressure, particularly headache and nausea, had the highest response rates.

Overall clinical response was achieved in 40 of 49 evaluable patients (81.6%; Table 3). Shunt malfunction requiring revision occurred in 2 patients (3.9%); no infections occurred.

Table 3
Neurologic Symptom Outcomes Following Cerebrospinal Fluid Shunting

Symptom	Improved	Persistent	Worsened	Evaluable	Improvement Rate
Headache	18	4	9	31	58.1
Nausea/Vomiting	10	2	4	16	62.5
Gait Disturbance	8	3	6	17	47.1
Cognitive Decline	7	9	5	21	33.3
Vision Symptoms	3	8	1	12	25
Urinary Incontinence	1	1	0	2	50

Post-Shunt Oncologic Therapy

After shunting, 41 patients (80.4%) received additional oncologic treatment. Combination therapy was administered to 29 patients (56.9%), a single modality to 12 (23.5%), and no further therapy to 10 (19.6%). CNS-penetrating therapies were administered to 20 patients (39.2%) (Supplementary table S3). Patients received a median of 1 post-shunt treatment line (IQR, 0–2; Table 4).

Table 4
Post-Shunt Oncologic Therapies Administered Following CSF
Diversion

Therapy	N	Total	Percent (%)
Any post-shunt therapy	41	51	80.4
Systemic chemotherapy	16	51	31.4
Targeted therapy	13	51	25.5
Immune checkpoint inhibitor	6	51	11.8
Intrathecal chemotherapy	3	51	5.9
Radiation	26	51	51
Combination therapy	29	51	56.9
CNS-penetrating agent	20	51	39.2

Overall Survival

At analysis, 42 patients had died. Median overall survival after shunting was 70 days (95% CI, 54–156 days). Receipt of post-shunt therapy was strongly associated with longer survival (Fig. 1). Median survival was 16 days without additional therapy, 75 days with a single modality, and 124 days with combination therapy (log-rank $p = 5 \times 10^{-9}$). CNS-penetrating therapy was also associated with longer survival. Median survival was 193 days among patients who received CNS-penetrating therapy versus 49 days among those who did not (log-rank $p = 0.0001$; Fig. 2). Among patients receiving any post-shunt therapy, median survival remained longer with CNS-penetrating therapy (193 versus 57 days; log-rank $p = 0.002$), suggesting that this benefit was not solely attributable to treatment selection. Survival also differed by CNS-active therapy and radiation exposure, with the longest survival among patients receiving CNS-active therapy alone (log-rank $p = 0.0017$; Fig. 3).

Brain Metastases and Intracranial Disease Burden

Brain metastases were present in 65% of patients. To examine metastatic burden, patients were classified as having no, solitary, or multiple (≥ 2) brain metastases. Median survival was 25.5 days among patients with brain metastases versus 104.5 days among those without. Although the Kaplan-Meier comparison did not reach significance (log-rank $p = 0.09$), this association persisted in Cox regression and remained significant after multivariable adjustment.

Tumor volume was available for 22 patients, who were stratified by the median volume of 4.56 cm³. Response and survival did not differ between high- and low-volume groups. Median survival was 48 and 75 days, respectively (log-rank $p = 0.90$), suggesting that volumetric disease burden was not a major determinant of outcome.

Disease Characteristics and Survival

Several disease characteristics were evaluated for associations with clinical response and survival (Supplementary Table S4). CSF cytology was associated with neither response (Fisher's exact $p = 0.69$) nor survival (log-rank $p = 0.60$). Similarly, diffuse versus nodular LMD pattern was associated with neither response ($p = 0.36$) nor survival (log-rank $p = 0.90$). Spinal involvement, prior CNS-directed therapy, and CNS treatment-naïve status were not associated with survival.

Cranial nerve involvement was an adverse prognostic factor. Although response rates did not differ by cranial nerve status (Fisher's exact $p = 0.68$), median survival was 57 days with cranial nerve involvement versus 75 days without (log-rank $p = 0.02$). Neither brain metastasis location nor LMD location was associated with survival (both $p = 0.80$; Supplementary Table S2).

Molecular Characteristics

Molecular data were available for selected tumor types (Supplementary Table S1). Among patients with breast cancer, 3 had HER2-positive and 6 had HER2-negative disease. Available subtypes included HER2-positive, hormone receptor-positive/HER2-negative, and triple-negative disease. Among patients with lung cancer, 2 had EGFR-mutant tumors; no ALK or ROS1 rearrangements were identified. Molecular data were limited among patients with melanoma. Overall, 13 patients (25.5%) had potentially actionable alterations. Actionable status was not associated with receipt of CNS-penetrating therapy ($p = 0.74$), clinical response ($p = 0.42$), or survival (log-rank $p = 0.30$). These analyses were limited by small subgroups and incomplete molecular testing.

Univariable Survival Analysis

Univariable Cox proportional hazards regression identified several factors associated with survival (Supplementary Table S4). Receipt of any post-shunt therapy was associated with substantially lower mortality (HR, 0.065; 95% CI, 0.021–0.196; $p < 0.001$). Systemic chemotherapy (HR, 0.48; 95% CI, 0.25–0.94; $p = 0.033$), combination therapy (HR, 0.45; 95% CI, 0.24–0.85; $p = 0.014$), and CNS-penetrating therapy (HR, 0.29; 95% CI, 0.15–0.56; $p < 0.001$) were also associated with longer survival.

Cranial nerve involvement (HR, 2.42; 95% CI, 1.11–5.26; $p = 0.026$) and a solitary brain metastasis (HR, 2.52; 95% CI, 1.06–6.00; $p = 0.037$) were associated with higher mortality. Histology, CSF cytology, MRI pattern, spinal involvement, radiation therapy, prior CNS treatment status, tumor volume, and actionable alterations were not significantly associated with survival.

Multivariable Survival Analysis

In multivariable Cox regression adjusted for baseline performance status, cranial nerve involvement remained independently associated with worse survival (HR, 4.25; 95% CI, 1.75–10.32; $p = 0.001$; Table 5). Brain metastasis was also associated with worse survival (HR, 2.86; 95% CI, 1.10–7.46; $p = 0.032$), whereas the number of brain metastases was not.

Table 5
Multivariable Cox Regression Analyses of Factors Associated with Overall Survival

Variable	HR	95% CI	p-value
KPS $\geq$ 60	0.51	0.25–1.02	0.057
Cranial nerve involvement	4.25	1.75–10.32	0.001
Brain metastasis	2.86	1.10–7.46	0.032
Any post-shunt therapy	0.078	0.022–0.282	< 0.001
CNS-penetrating therapy	0.266	0.116–0.612	0.002

Receipt of any post-shunt therapy remained the strongest predictor of longer survival (HR, 0.078; 95% CI, 0.022–0.282; $p < 0.001$). CNS-penetrating therapy was also independently associated with longer survival (HR, 0.266; 95% CI, 0.116–0.612; $p = 0.002$). KPS $\geq$ 60 showed a nonsignificant trend toward longer survival (HR, 0.51; $p = 0.057$).

Sensitivity Analysis

Substituting ECOG performance status for KPS produced similar results (Supplementary Table S5). Cranial nerve involvement (HR, 3.65; $p = 0.004$), brain metastasis (HR, 2.86; $p = 0.037$), post-shunt therapy (HR, 0.070; $p < 0.001$), and CNS-penetrating therapy (HR, 0.298; $p = 0.004$) remained independently associated with survival, supporting the primary findings.

Discussion

In this single-center study of 51 patients undergoing CSF shunting for LMD-associated hydrocephalus, median survival was 70 days and symptomatic improvement occurred in 81.6%. Median survival reached 193 days among patients receiving CNS-penetrating therapy. These findings support CSF diversion as palliation and a potential bridge to oncologic therapy.

Symptomatic Benefit of CSF Shunting

The 81.6% improvement rate is consistent with systematic reviews and meta-analyses of more than 1,500 patients, which reported improvement in approximately 75–80% after CSF diversion, particularly for headache and nausea/vomiting[4], [11], [12]. Large institutional series have similarly reported improvement in more than 80%[10].

Headache (58.1%) and nausea/vomiting (62.5%) had the highest response rates, whereas cognitive decline (33.3%) and visual symptoms (25.0%) improved less frequently. This likely reflects the greater reversibility of pressure-mediated symptoms than deficits caused by leptomeningeal or cranial nerve infiltration[1], [5]. Shunting enabled 80.4% of patients to receive additional therapy, supporting its role as both palliation and a bridge to treatment[10], [14].

Overall Survival and Comparison With Published Data

Median survival after shunting was 70 days (2.3 months), at the lower end of published estimates. Meta-analyses report approximately 3–5 months, while institutional series report 2.4–3.9 months[9], [10], [11], [12], [14], [15], [16]. This difference may reflect the inclusion of patients with advanced disease and broader use of shunting in this population[10].

CNS-Penetrating Therapy as a Key Determinant of Survival

CNS-penetrating therapy was independently associated with longer survival (HR, 0.27; 95% CI, 0.12–0.61; $p = 0.002$), with median survival of 193 versus 49 days. This aligns with evidence supporting CNS-active systemic therapies in LMD, including osimertinib in EGFR-mutant non-small cell lung cancer[10]. CNS-active targeted therapy has similarly predicted longer survival among shunted patients[17] and is increasingly emphasized in contemporary guidelines[18], [19], [20], [21]. Exploratory analyses suggested that this benefit was driven primarily by CNS-active systemic therapy rather than radiation[22], [23]. Although radiation remains important for palliation of focal or bulky disease, its addition may not improve survival when effective CNS-active therapies are available[24], [25], [26].

Prognostic Significance of Cranial Nerve Involvement and Brain Metastases

Cranial nerve involvement was a strong adverse prognostic factor, conferring a more than fourfold higher mortality risk (adjusted HR, 4.25; $p = 0.001$). This finding aligns with evidence that cranial nerve deficits reflect advanced leptomeningeal spread and are recognized as poor-risk features in NCCN guidelines[2], [19], [27]. Brain metastases were also independently associated with worse survival (HR, 2.86; $p = 0.032$), consistent with studies demonstrating poorer outcomes with concomitant parenchymal CNS disease[10], [28], [29]. However, intracranial tumor volume was not associated with survival, suggesting that the presence of brain metastases may be more prognostically relevant than their volumetric burden.

Factors Not Associated With Survival

Several variables traditionally considered prognostic in LMD were not associated with survival, including CSF cytology, MRI pattern (diffuse versus nodular), spinal involvement, and actionable molecular alterations[30]. The lack of prognostic significance for CSF cytology contrasts with the EANO–ESMO classification, which distinguishes confirmed cytology-positive LMD (type I) from probable or possible LMD (type II) and has demonstrated prognostic validity in larger cohorts[31], [32]. These null findings may reflect the limited sample size and the specific population selected for shunting, which may represent a more uniformly advanced disease group.

Limitations

This study has several limitations. Its retrospective, single-center design introduces selection and information biases. The sample of 51 patients limits statistical power, particularly for subgroup and interaction analyses, and increases the risk of type I and II errors. The association between post-shunt

therapy and survival is susceptible to immortal time bias because patients who survived longer had greater opportunity to receive treatment. Formal RANO-LM response criteria could not be applied because standardized serial assessments were unavailable. Molecular profiling was incomplete, limiting biomarker analyses. Finally, heterogeneity in primary tumors and treatment regimens, while reflecting real-world practice, limits generalizability to specific histologic subgroups.

Conclusions

CSF shunting for LMD-associated hydrocephalus provided meaningful symptomatic improvement in most patients and facilitated further oncologic therapy. CNS-penetrating therapy was associated with longer survival, although potential immortal time bias warrants cautious interpretation. Cranial nerve involvement and brain metastases were adverse prognostic factors that may inform counseling and treatment planning. Prospective multicenter studies incorporating standardized response assessments and molecular stratification are needed to refine patient selection and optimize the integration of CSF diversion with contemporary systemic therapies.

Declarations

Disclosures:

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

Funding:

No funding was received for the preparation of this manuscript.

Author Contribution

Author Contributions: Conceptualization: KGA, MTG; Data collection: MTG, NNG; Data analysis: KGA, MTG; Writing – original draft: KGA, MTG, NNG, KM, FY; Writing – review & editing: KGA, MTG, KM, FY, POZ; Supervision: KGA.

Data Availability

All data supporting the findings of this study are available within the paper and its Supplementary Information.

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Figures

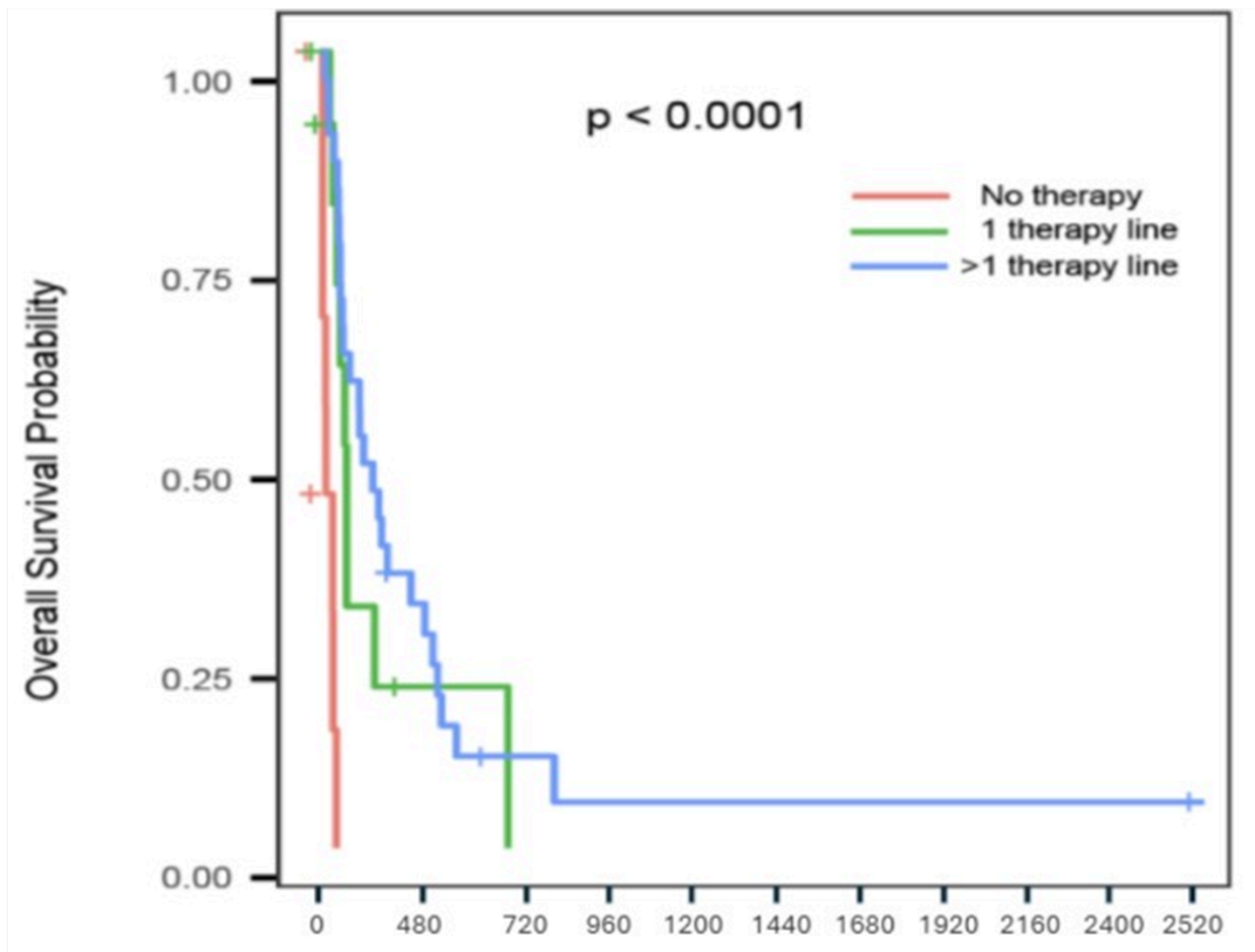


Figure 1

Overall survival according to post-shunt treatment intensity (none, single modality, combination therapy)

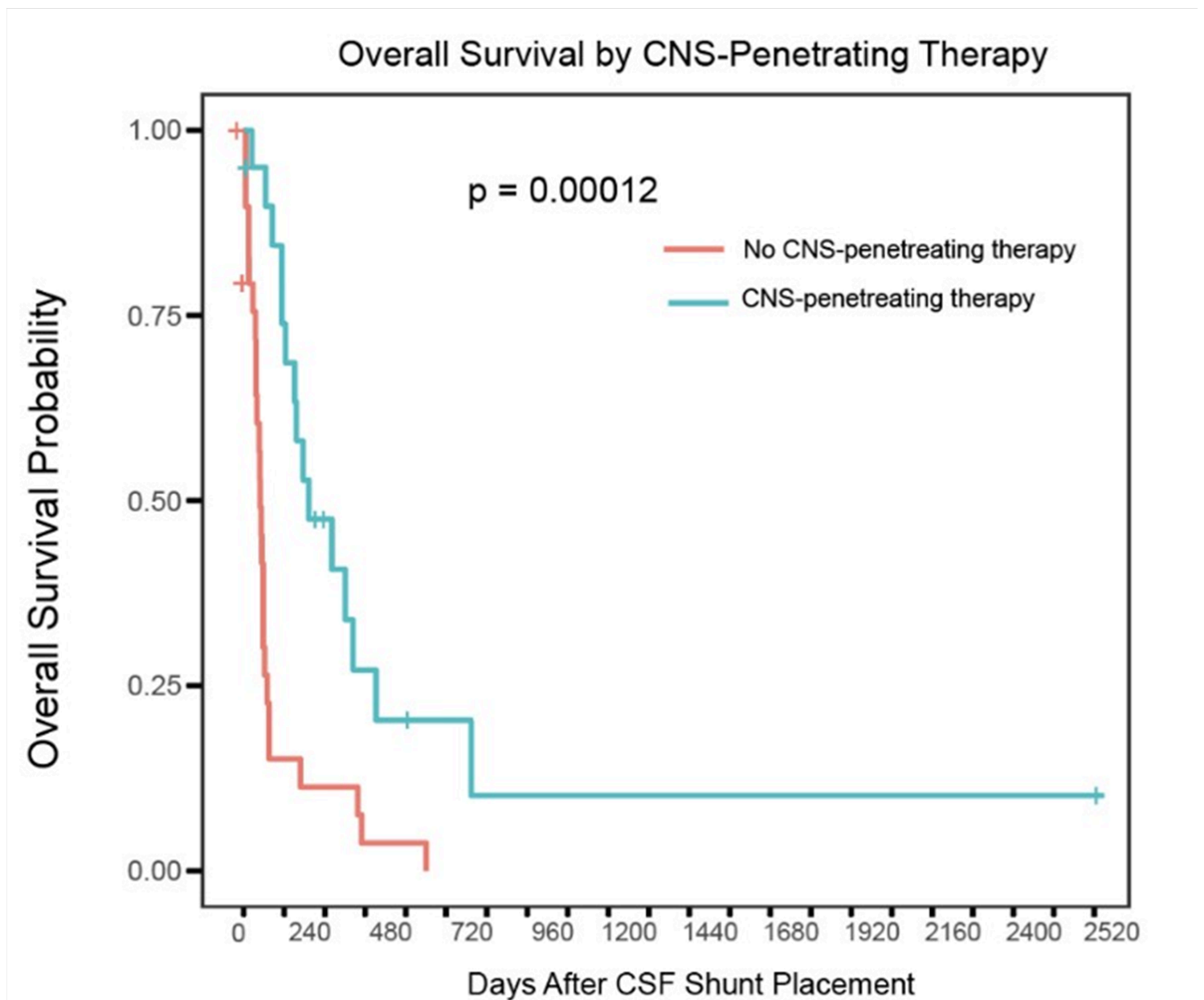


Figure 2

Overall survival according to receipt of CNS-penetrating therapy

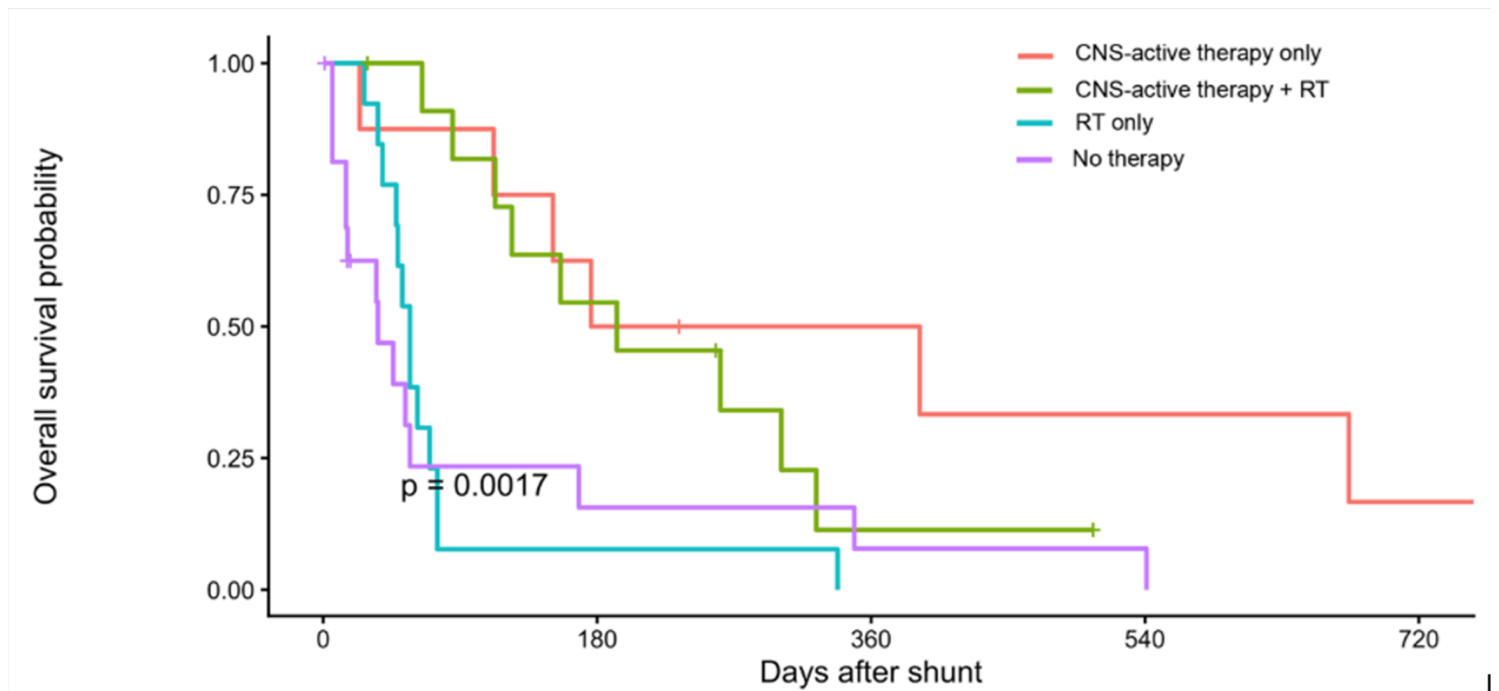


Figure 3

Overall survival according to CNS-active therapy and radiation exposure

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