BRAIN CANCER TREATMENT REGIMENS (Part 1 of 9)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Systemic Therapy for Adult Low-Grade Infiltrative Supratentorial Astrocytoma/Oligodendroglioma[1]

Note: All recommendations are Category 2A unless otherwise indicated.

Adjuvant Treatment

REGIMEN	DOSING
Combination PCV (lomustine + procarbazine + vincristine) (Category 1)[2]	**Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.
Temozolomide[3–5]	**Days 1–49:** Temozolomide 75mg/m² orally. Repeat cycle every 11 weeks (7 weeks on/4 weeks off) for 6 cycles. **OR** **For children/adolescents:** Temozolomide monthly 5-day courses at doses of 200mg/m²/day (patients with no prior craniospinal irradiation [CSI]) or 180mg/m²/day (prior CSI). **OR** **Days 1–21:** Temozolomide 75mg/m²/day orally. Repeat cycle every 28 days.

Recurrent or Progressive, Low Grade Disease

Temozolomide[3,6a]	**Days 1–49:** Temozolomide 75mg/m² orally. Repeat cycle every 11 weeks (7 weeks on/4 weeks off) for 6 cycles. **OR** **Days 1–5:** Temozolomide 150mg/m² to 200mg/m²; when patients progress during conventional temozolomide treatment, change temozolomide to a 50mg/m² daily regimen. Repeat cycle every 28 days.
Combination PCV regimens (lomustine + procarbazine + vincristine)[7]	**Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.
Platinum-based regimen: Carboplatin[8]	**Day 1:** Carboplatin 350mg/m² IV **Days 1–3:** Teniposide 50mg/m² IV. Repeat cycle every 4 weeks.
Platinum-based regimen: Carboplatin[9]	Carboplatin 560mg/m² IV at 4-week intervals; continued until disease progression, unacceptable toxicity, or for 12 additional courses after achieving maximal response.
Platinum-based regimen: Cisplatin[10]	**Days 1–3:** Cisplatin 25mg/m²/day IV + etoposide 100mg/m²/day IV. Repeat cycle every 4 weeks for first 3 cycles, then repeat every 5 weeks for next 3 cycles, then repeat every 6 weeks for the last 3 cycles; total 10 cycles over approximately 10–11 months (total dose 750mg/m² cisplatin and 3,000mg/m² etoposide).
Lomustine[11]	Lomustine 130mg/m² orally every 6 weeks.
Carmustine[12]	Carmustine 150–200mg/m² IV as a single dose or divided over 2 days given every 6 weeks OR 75–100mg/m²/day IV for 2 days every 6 weeks.

Systemic Therapy for Anaplastic Gliomas[1]

Adjuvant Treatment

Temozolomide[13,14]	**Days 1–5:** Temozolomide 200mg/m²/day orally. Repeat cycle every 4 weeks until disease progression or for up to 24 cycles.
PCV with deferred RT[13]	**Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.
Concurrent temozolomide (with RT)[15]	2 Gy given 5 days/week for 6 weeks plus continuous daily oral temozolomide (75mg/m²/day, 7 days per week from the first to the last day of radiotherapy), followed by 6 cycles of adjuvant temozolomide 150–200mg/m²/day for 5 days. Repeat cycle every 28 days.

continued

Systemic Therapy for Anaplastic Gliomas[1] (continued)

Recurrence Therapy

REGIMEN	DOSING
Temozolomide[4,6,16]	Temozolomide 50mg/m² daily for up to 1 year or until disease progression. **OR** **For children/adolescents:** Temozolomide monthly 5-day courses at doses of 200mg/m²/day (patients with no prior CSI) or 180mg/m²/day (prior CSI). **OR** **Days 1–5:** Temozolomide 150mg/m² to 200mg/m² 5 days of each 28-day cycle; when patients progress during conventional temozolomide treatment, change temozolomide to a 50mg/m² daily regimen. **OR** **Days 1–5:** Temozolomide 150mg/m² to 200mg/m². Repeat cycle every 28 days.
Lomustine or carmustine[11,12,17]	**Day 1:** Lomustine 100–130mg/m²/day orally. Repeat cycle every 6 weeks. **OR** Carmustine 150–200mg/m² IV as a single dose or divided over 2 days given every 6 weeks OR 75–100mg/m²/day IV for 2 days every 6 weeks.
Combination PCV regimens (lomustine + procarbazine + vincristine)[7]	**Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.
Bevacizumab[18–20b]	**Day 1:** Bevacizumab 10mg/kg IV. Repeat cycle every 14 days.
Bevacizumab + irinotecan[21,22c]	**Day 1:** Bevacizumab 10mg/kg IV plus irinotecan 125mg/m² IV. Repeat cycle every 2 weeks. **OR** Bevacizumab 10mg/mg² IV plus irinotecan 340mg/m² IV in patients receiving enzyme-inducing antiepileptic drugs (EIAED). Repeat cycle every 14 days.
Bevacizumab + nitrosurea[23]	**Days 1 and 15:** Bevacizumab 10mg/kg IV **Days 1 and 8:** Fotemustine 75mg/m² IV Followed after a 3-week interval by a maintenance phase of bevacizumab 10mg/kg IV plus fotemustine 75mg/m² IV. Repeat cycle every 3 weeks.
Bevacizumab + carboplatin (Category 2B)[24,25]	**Day 1:** Bevacizumab 10mg/kg IV plus carboplatin AUC 4–6mg•min/mL, depending on the patient's prior treatment history and bone marrow reserves; cycle 2 doses of carboplatin (every 28 days) and 3 doses of bevacizumab (every 14 days) and lasted 6 weeks.
Irinotecan[26,27]	**Day 1:** Irinotecan 350mg/m² IV to patients on non-enzyme-inducing antiepileptic drugs (NEIAED) or 600mg/m² to patients on EIAED. Repeat cycle every 21 days. **OR** **Day 1:** Irinotecan 350mg/m² IV. Repeat cycle every 21 days.
Platinum-based regimen: Carboplatin[8]	**Day 1:** Carboplatin 350mg/m² IV **Days 1–3:** Teniposide 50mg/m² IV. Repeat cycle every 4 weeks.
Platinum-based regimen: Carboplatin[9]	Carboplatin 560mg/m² IV at 4-week intervals; continued until disease progression, unacceptable toxicity, or for 12 additional courses after achieving maximal response.
Platinum-based regimen: Cisplatin[10]	**Days 1–3:** Cisplatin 25mg/m²/day IV + etoposide 100mg/m²/day IV. Repeat cycle every 4 weeks for first 3 cycles, then repeat every 5 weeks for next 3 cycles, then repeat every 6 weeks for the last 3 cycles; total 10 cycles over approximately 10–11 months (total dose 750mg/m² cisplatin and 3,000mg/m² etoposide).
Cyclophosphamide (Category 2B)[28,29]	**Days 1–2:** Cyclophosphamide 750mg/m² IV. Repeat cycle every 28 days.
Etoposide[30]	Etoposide 50mg/day IV given until the neutrophil count dropped to $< 1.0 \times 10^9$/L or the platelets fell to $< 75 \times 10^9$/L and resumed when the counts rose to normal levels.

continued

BRAIN CANCER TREATMENT REGIMENS (Part 3 of 9)

Systemic Therapy for Anaplastic Oligoastrocytoma[1]

Adjuvant Treatment

REGIMEN	DOSING
Radiotherapy + PCV for 1p19q co-deleted (Category 1)[31]	59.6 4 Gy of RT, followed by 6 cycles of standard PCV: **Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.

Systemic Therapy for Glioblastoma[1]

Adjuvant Treatment

Concurrent temozolomide (with RT)[15]	2 Gy given 5 days/week for 6 weeks plus continuous daily oral temozolomide (75mg/m²/day, 7 days per week from the first to the last day of radiotherapy), followed by 6 cycles of adjuvant temozolomide 150–200mg/m²/day for 5 days. Repeat cycle every 28 days.
Post-RT temozolomide[32]	**Days 1–5:** Temozolomide 150–200mg/m²/day orally for 5 days. Repeat cycle every 28 days.
Temozolomide + standard RT[33]	**Days 1–5:** Temozolomide 200mg/m², orally plus: Standard RT: 60.0 Gy administered in 2.0 Gy fractions over 6 weeks.

Recurrence Therapy

Bevacizumab[34–36b]	**Day 1:** Bevacizumab 10mg/kg IV. Repeat cycle every 14 days.
Bevacizumab + irinotecan[22,34–36c]	**Day 1:** Bevacizumab 10mg/kg IV. Repeat cycle every 14 days. After tumor progression, immediately treat with bevacizumab 10mg/kg IV plus irinotecan 340mg/m² or 125mg/m² IV every 14 days, depending on use of EIAEDs.
Bevacizumab + nitrosurea[23c]	**Days 1 and 15:** Bevacizumab 10mg/kg IV **Days 1 and 8:** Fotemustine 75mg/m² IV Followed after a 3-week interval by a maintenance phase of bevacizumab 10mg/kg IV plus fotemustine 75mg/m² IV. Repeat cycle every 3 weeks.
Bevacizumab + carboplatin (Category 2B)[24,25c]	**Day 1:** Bevacizumab 10mg/kg IV plus carboplatin AUC 4–6mg•min/mL, depending on the patient's prior treatment history and bone marrow reserves; cycle 2 doses of carboplatin (every 28 days) and 3 doses of bevacizumab (every 14 days) for 6 weeks.
Temozolomide[6,32,37]	**Days 1–5:** Temozolomide 150mg/m² to 200mg/m²; when patients progress during conventional temozolomide treatment, change temozolomide to a 50mg/m² daily regimen. Repeat cycle every 28 days. **OR** 2 Gy given 5 days/ week for 6 weeks plus continuous daily oral temozolomide (75mg/m²/day, 7 days per week from the first to the last day of radiotherapy), followed by 6 cycles of adjuvant temozolomide 150–200mg/m²/day for 5 days. Repeat cycle every 28 days. **OR** **Chemotherapy-naive patients:** **Days 1–5:** Temozolomide 200mg/m²/day. **Chemotherapy-experienced patients:** **Days 1–5:** Temozolomide 150mg/m²/day, increasing to 200mg/m²/day in the absence of grade 3/4 toxicity. Repeat cycle every 28 days.
Lomustine or carmustine[11,12,17]	**Day 1:** Lomustine 100–130mg/m²/day orally. Repeat cycle every 6 weeks. **OR** Carmustine 150–200mg/m² IV as a single dose or divided over 2 days given every 6 weeks **OR** 75–100mg/m²/day IV for 2 days every 6 weeks.
Combination PCV regimens (lomustine + procarbazine + vincristine)[7]	**Day 1:** Lomustine 110mg/m² orally **Days 8–21:** Procarbazine 60mg/m² orally once daily **Days 8 and 29:** Vincristine 1.4mg/m² (maximum 2mg) IV. Repeat every 6 weeks.
Cyclophosphamide (Category 2B)[28]	**Days 1–2:** Cyclophosphamide 750mg/m² IV. Repeat cycle every 28 days.

continued

BRAIN CANCER TREATMENT REGIMENS (Part 4 of 9)

Systemic Therapy for Glioblastoma[1] (continued)

Recurrence Therapy (continued)

REGIMEN	DOSING
Platinum-based regimen: Carboplatin[8]	**Day 1:** Carboplatin 350mg/m² IV **Days 1–3:** Teniposide 50mg/m² IV. Repeat cycle every 4 weeks.
Platinum-based regimen: Carboplatin[9]	Carboplatin 560mg/m² IV at 4-week intervals; continued until disease progression, unacceptable toxicity, or for 12 additional courses after achieving maximal response.
Platinum-based regimen: Cisplatin[10]	**Days 1–3:** Cisplatin 25mg/m²/day IV + etoposide 100mg/m²/day IV. Repeat cycle every 4 weeks for first 3 cycles, then repeat every 5 weeks for next 3 cycles, then repeat every 6 weeks for the last 3 cycles; total 10 cycles over approximately 10–11 months (total dose 750mg/m² cisplatin and 3,000mg/m² etoposide).

Systemic Therapy for Intracranial and Spinal Ependymoma (excluding supependymoma)[1]

Recurrence Therapy

Platinum-based regimen: Carboplatin[8]	**Day 1:** Carboplatin 350mg/m² **Days 1–3:** Teniposide 50mg/m². Repeat cycle every 4 weeks.
Platinum-based regimen: Carboplatin[9]	Carboplatin 560mg/m² IV at 4-week intervals; continued until disease progression, unacceptable toxicity, or for 12 additional courses after achieving maximal response.
Platinum-based regimen: Cisplatin[10]	**Days 1–3:** Cisplatin 25mg/m²/day IV + etoposide 100mg/m²/day IV. Repeat cycle every 4 weeks for first 3 cycles, then repeat every 5 weeks for next 3 cycles, then repeat every 6 weeks for the last 3 cycles; total 10 cycles over approximately 10–11 months (total dose 750mg/m² cisplatin and 3,000mg/m² etoposide).
Etoposide[30]	Etoposide 50mg/day given until the neutrophil count dropped to $<1.0 \times 10^9$/L or the platelets fell to $<75 \times 10^9$/L and resumed when the counts rose to normal levels.
Bevacizumab[34–37b]	**Day 1:** Bevacizumab 10mg/kg IV. Repeat cycle every 14 days.
Temozolomide[3–5]	**Days 1–49:** Temozolomide 75mg/m² orally. Repeat cycle every 11 weeks (7 weeks on/4 weeks off) for 6 cycles. **OR** **Days 1–21:** Temozolomide 75mg/m²/day orally. Repeat cycle every 28 days.

Systemic Therapy for Adult Medulloblastoma and Supratentorial Primitive Neuroectodermal Tumor (PNET)[1]

Adjuvant Treatment

Weekly vincristine during craniospinal radiation therapy followed by either of the following regimens. Note that omission of vincristine during radiation therapy phase of therapy or dose modification may be required for adults because they do not tolerate this regimen as well. Data supporting the use of vincristine has been found in pediatric trials only. Patients should be closely monitored for neurologic toxicity with periodic exams.

Vincristine + cisplatin + lomustine[38]	During craniospinal radiotherapy (RT) **Day 1:** Lomustine 75mg/m² orally **Day 2:** Cisplatin 75mg/m² IV **Days 2, 8 and 15:** Vincristine 1.5mg/m² IV bolus, max 2mg bolus; up to max 8 doses.
Vincristine + cisplatin + cyclophosphamide[39]	**Day 1:** Cisplatin 75mg/m² IV **Days 2, 8 and 15:** Vincristine 1.5mg/m² IV bolus, max 2mg bolus **Days 22, 23:** Cyclophosphamide 1,000mg/m² IV.

Recurrence Therapy

No prior chemotherapy: Consider high-dose chemotherapy with autologous stem cell reinfusion in patients who achieve a complete remission with conventional doses of salvage chemotherapy or have no residual disease after re-resection.[35]

High dose cyclophosphamide ± etoposide

Carboplatin + etoposide + cyclophosphamide

Cisplatin + etoposide + cyclophosphamide

Prior chemotherapy: Consider high-dose chemotherapy with autologous stem cell reinfusion in patients who achieve a complete remission with conventional doses of salvage chemotherapy or have no residual disease after re-resection.[35]

High dose cyclophosphamide ± etoposide

Temozolomide[3]	Temozolomide 75mg/m² orally in 11-week cycles of 7 weeks on followed by 4 weeks off.
Oral etoposide[40,41]	**Days 1–21:** Etoposide 50mg orally daily. Repeat cycle every 4 weeks.

continued

BRAIN CANCER TREATMENT REGIMENS (Part 5 of 9)

Primary CNS Lymphoma[1]

Primary Treatment

REGIMEN	DOSING
High dose methotrexate + chemotherapy[42–44]	**High dose methotrexate combined with the following plus radiation therapy:** **Weeks 1, 3, 5, 7, and 9:** MTX 2.5g/m² + vincristine 1.4mg/m² with a cap of 2.8mg (2m²) **Weeks 1, 5, and 9:** Procarbazine 100mg/m²/day orally for 7 days **Weeks, 2, 4, 6, 8, and 10:** Methotrexate 12mg intraventricularly **Weeks 1, 3, 5, 7, and 9:** Leucovorin 20mg every 6 hours orally for 12 doses **Weeks, 2, 4, 6, 8, and 10:** Leucovorin 10mg orally twice daily for 8 doses **Weeks 11–15:** Whole-brain RT in 1.80-Gy fractions for a total dose of 45 Gy **Weeks 16 and 19:** Cytarabine 3mg/m²/day IV for 2 days. Repeat for 5 cycles. **OR** **Day 1:** MTX 3.5g/m² **Days 2–3:** Cytarabine 2g/m² IV twice a day. **OR** **Day 1:** MTX 4gm/m² IV, followed by leucovorin 20–25mg IV every 6 hours starting 24 hours after MTX for 72 hours or until serum MTX level <1 × 10–8mg/dL. Increase leucovorin to 40mg every 4 hours if MTX level >1 × 10–5mg/dL at 48 hours or >1 × 10–8mg/dL at 72 hours. **Days 3–5:** Ifosfamide 1.5gm/m² IV + mesna 400mg IV before ifosfamide, then 4 hours and 8 hours after.
High dose methotrexate (MTX 2.5–4.0mg/m²) + chemotherapy ± monoclonal antibody[45]	**Day 1:** Rituximab 500mg/m² IV **Day 2:** MTX 3.5mg/m² IV plus vincristine 1.4mg/m² Procarbazine 100mg/m²/day was administered for 7 days with odd-numbered cycles.
High dose methotrexate (MTX 8.0mg/m²) + chemotherapy ± monoclonal antibody[46–47]	**High dose methotrexate combined with the following plus radiation therapy deferred radiation therapy:** **Induction therapy** MTX 8g/m² IV administered every 2 weeks until complete response achieved or max of 8 cycles reached. **Consolidation** MTX 8g/m² IV administered every 2 weeks for 2 cycles. **Maintenance therapy** MTX 8g/m² IV administered every 4 weeks for 11 cycles. **Plus** **Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 4 weeks for 4 cycles. **OR** **Induction therapy** **Day 1:** Rituximab 375mg/m² IV, **followed by** **Days 1–5:** Temozolomide 150–200mg/m² orally daily, after rituximab infusion. Repeat cycle every 4 weeks for 4 cycles. **Maintenance therapy** **Days 1–5:** Temozolomide 150–200mg/m² orally daily. Repeat cycle every 4 weeks for 8 cycles.
Consider urgent glucarpidase (carboypeptidase G2) for prolonged MTX clearance due to MTX-induced renal toxicity[48]	Glucarpidase, one 50U/kg dose IV, 2 doses 24 hours apart, or 3 doses every 4 hours; thymidine 8 g/m²/day IV administered as continuous IV infusion for ≥48 hours after the last dose of glucarpidase; leucovorin 1g/m² IV every 6 hours before administration of glucarpidase and at a dose of 250mg/m² IV every 6 hours for 48 hours after administration of the last dose of glucarpidase.

Recurrent or Progressive Disease

Consider high-dose chemotherapy with autologous stem cell reinfusion in patients who achieve a complete remission with conventional doses of salvage chemotherapy or have no residual disease after re-resection.[35]

Re-treat with high-dose methotrexate[46]	**Induction therapy** MTX 8g/m² IV administered every 2 weeks until complete response achieved or max of 8 cycles reached. **Consolidation** MTX 8g/m² IV administered every 2 weeks for 2 cycles. **Maintenance therapy** MTX 8g/m² IV administered every 4 weeks for 11 cycles.

continued

BRAIN CANCER TREATMENT REGIMENS (Part 6 of 9)

Primary CNS Lymphoma[1] (continued)

Recurrent or Progressive Disease (continued)

REGIMEN	DOSING
Rituximab ± temozolomide[49]	**Induction therapy** **Day 1:** Rituximab 375mg/m² IV, **±** **Days 1–5:** Temozolomide 150–200mg/m² orally daily, administered after rituximab infusion. Repeat cycle every 4 weeks for 4 cycles. **Maintenance therapy** **Days 1–5:** Temozolomide 150–200mg/m² orally daily, administered after rituximab infusion. Repeat cycle every 4 weeks for 8 cycles.
Topotecan[50]	**Days 1–5:** Topotecan 1.5mg/m² IV. Repeat cycle every 21 days.
High-dose cytarabine[51]	Cytarabine 3g/m² IV.
Dexamethasone + high-dose cytarabine + cisplatin[52]	**Day 1:** Cisplatin 100mg/m² continuous IV infusion over 24 hours, followed by 2 pulses each of cytarabine at a dose of 2g/m² given 12 hours apart. **Days 1–4:** Dexamethasone 40mg PO or IV. Repeat cycle every 3–4 weeks for 6–10 courses.
Pemetrexed[53]	Pemetrexed 900mg/m² IV every 21 days for 6 weeks.

Meningioma[1]

Interferon-alfa (Category 2B)[54]	α-IFN 106 units/m² SC every other day for 4 weeks. Repeat cycle every 4 weeks.
Somatostatin analog[55]	Sandostatin LAR Depot 10–30mg IM every 4 weeks.
Sunitinib (Category 2B)[56]	**Days 1–28:** Sunitinib 50mg orally daily. Repeat cycle every 42 days.

Systemic Therapy for Limited (1–3) Metastatic or Multiple (>3) Metastatic Lesions[1]

Recurrent disease—Treatment as per the regimens of the primary tumor (‡ Bevacizumab + chemotherapy can be considered for patients who have failed monotherapy with bevacizumab)

Carmustine wafer[57]	8 wafers (7.7mg) for a total of 61.6mg implanted intracranially.
High-dose methotrexate (MTX; breast and lymphoma)[58,59]	**Breast:** MTX 3.5g/m² IV. **Lymphoma:** Treatment based on weekly high-dose MTX 3.5g/m² and weekly intra-CSF cytarabine; oral procarbazine 100mg/m² days 2–15 was added to patients whose bone marrow reserve could tolerate this drug.
Capecitabine ± lapatinib, cisplatin, etoposide[60–68]	**Days 1–14:** lapatinib 1,250mg orally plus capecitabine 1,000mg/m² orally twice per day. Repeat cycle every 21 days. **OR** **Days 1–14:** Capecitabine 2,000mg/m²/day in 2 divided doses for 14 days, followed by a 7-day rest and lapatinib 1,250mg once daily continuously. **OR** **Day 1:** Cisplatin 100mg/m² IV **Days 4, 6, and 8:** Etoposide 100mg/m². Repeat cycle every 21 days. **OR** **Day 1:** Cisplatin 100mg/m² IV **Days 1, 3, and 5 OR Days 4, 6, and 8:** Etoposide 100mg/m² IV. Repeat cycle every 21 days. **OR (breast)** Capecitabine orally starting at a dose of 1,800mg/m²/day (up to 2,000mg/m²/day) in 2 divided doses, and temozolomide given orally once daily at a starting dose of 75mg/m²/day. Concomitant daily doses given on days 1–5 and days 8–12, with cycles repeated every 21 days until disease progression. **OR (breast)** **Days 1–14:** Capecitabine 2,000mg/m²/day orally once daily. Repeat cycle every 21 days. **OR (breast)** **Days 1–21:** Capecitabine 2,400mg/m²/day orally once daily. Repeat cycle every 28 days.
Ipilimumab (melanoma)[69]	**Day 1:** Ipilimumab 10mg/kg IV. Repeat cycle every 21 days for a maximum 4 cycles. Individuals who were clinically stable at week 24 were eligible to receive ipilimumab 10mg/kg every 12 weeks.

continued

BRAIN CANCER TREATMENT REGIMENS (Part 7 of 9)

Systemic Therapy for Limited (1–3) Metastatic or Multiple (>3) Metastatic Lesions[1] (continued)

REGIMEN	DOSING
BRAF inhibitors (melanoma): Dabrafenib[70]	Dabrafenib 150mg orally twice daily.
BRAF inhibitors (melanoma): Vemurafenib[71]	Vemurafenib 960mg orally twice daily.
Topotecan (small cell lung)[50]	**Days 1–5:** Topotecan 1.5mg/m² IV over 30 minutes. Repeat cycle every 21 days.

Systemic Therapy for Leptomeningeal Metastases[1]

Organ-specific Systemic Chemotherapy; Emphasizing Drugs with Good CNS Penetration

Intra-CSF chemotherapy: Liposomal (slow-release) cytarabine (lymphoma/ leukemias)[72,73]	**Induction** Liposomal cytarabine 50mg intrathecally once every 14 days for 2 doses. **Maintenance** Liposomal cytarabine 50mg every 14 days for 2 doses, followed by 50mg every 28 days for 2 doses. **OR** **Induction** Liposomal cytarabine 50mg intraventricularly every 14 days for 3 doses plus rituximab 25mg intraventricularly twice per week for 8 doses. **Maintenance** Liposomal cytarabine 50mg intraventricularly once weekly plus rituximab 25mg intraventricularly twice weekly for 4 weeks. Repeat cycle every 4 weeks until disease progression
Intra-CSF chemotherapy: topotecan[74]	Topotecan 400 µg intraventrically twice weekly for 6 weeks.
Intra-CSF chemotherapy: etoposide[75]	**Induction** **Days 1–5:** Etoposide 0.5mg/day intra-CSF every other week for 8 weeks. **Maintenance** **Days 1–5:** Etoposide 0.5mg/day every 4 weeks.
Intra-CSF chemotherapy: trastuzumab[76]	Cumulative dose of intrathecal trastuzumab given in clinical studies was 1,040mg (SD 697.9, median 1,215, range 55–1,675)
Intra-CSF chemotherapy: Interferon-alfa (category 2B)[77]	IFN-α 1 × 106 IU subcutaneously every other day 3 times per week for 4 weeks by induction.
High-dose methotrexate for lymphoma and breast[58]	**Breast:** MTX 3.5g/m² IV.
Erlotinib (Category 2B)[78]	Weekly pulse erlotinib for EGFR exon 19 or exon 21 L858R mutation non-small cell lung cancer; trial demonstrates that a new schedule of erlotnib administration may overcome acquired resistance to erlotinib. Pulsatile high-dose erlotinib was found to be effective against brain metastases in patients who had progressed while on treatment with standard-dose erlotinib. Pulsatile high-dose erlotinib 1,500mg (median dose with range of 900–1,500mg) once weekly.

Systemic Therapy for Metastatic Spine Tumors[1]

Use regimen for disease specific site

a For patients not previously treated

b Patients who have good performance status but evidence of radiographic progression may benefit from continuation of bevacizumab to prevent rapid neurologic deterioration

c Bevacizumab + chemotherapy can be considered for patients who have failed monotherapy with bevacizumab

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