Mise à jour des recommandations dans les LPT

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Niveaux de recommandation

Levels of evidence

I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well- conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, expert opinions

Grades of recommendation

A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

Pronostic

- For CD20-positive polymorphic and monomorphic PTLD (NHL), the **IPI** remains the most appropriate prognostic score. (IV, B)

- CNS involvement, T-cell PTLD, and plasmablastic PTLD are associated with a more guarded prognosis. (IV, C)

Imagerie : Diagnostic – Evaluation

- In adults, positron emission tomography (**PET CT** scan) is the preferred imaging modality for diagnosis (IV, A).

- In children, either CT or PET-CT can be used for diagnosis; if the examination is negative and PTLD suspicion remains high, alternative imaging modalities may be considered (V, C).

- The assessment of **response** after four rituximab treatments in polymorphic PTLD and lymphoma should preferably be performed using **PET-CT** (IV, B).

- The benefit of systematic imaging follow-up after complete remission remains controversial and is not universally recommended (V, D).

- For PTLD involving the **central nervous system**, magnetic resonance imaging **(MRI) with gadolinium** contrast is the imaging modality of choice (IV, A).

Prophylaxie

- For an **EBV negative patient**, an **EBV negative donor** is preferred (III, B).
- No prophylactic treatment is recommended (IV, C).
- Due to currently insufficient prospective data, **rituximab prophylaxis is not recommended** (IV, C).

Traitement préemptif

1- Charge virale EBV

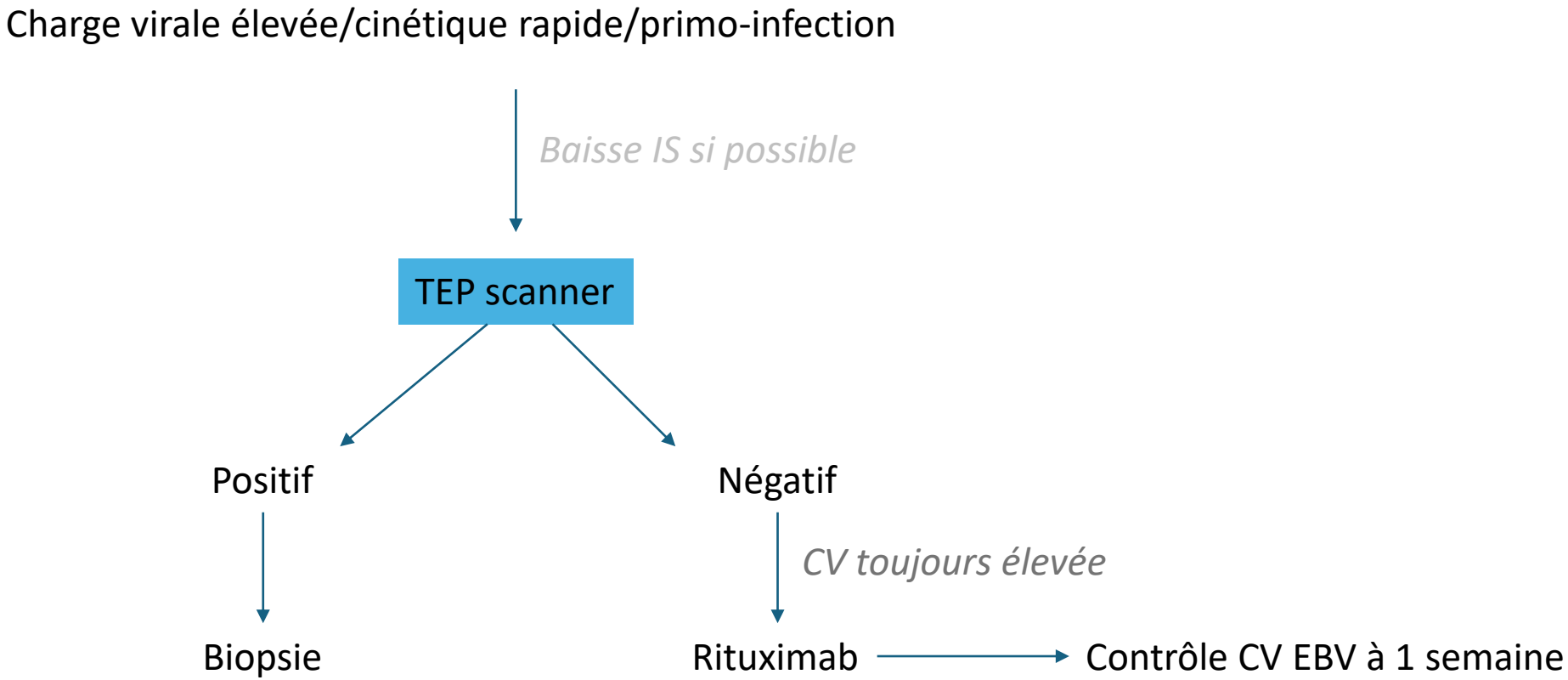
- EBV viral load measurement should be performed **on whole blood** (III, A).
- Viral load monitoring for a given patient should be conducted in the **same laboratory** using the same technique (III, B).
- EBV viral load may be expressed either in copies/mL or in IU/mL (III, B).
- When viral load comparisons between different laboratories are required, results should preferably be expressed in IU/mL (III, B).
- **EBV viral load monitoring is necessary in patients at high risk for PTLD** (e.g., EBV D+R–, high-risk post-HSCT according to Storek 2023, and intestinal transplant recipients) (III, A).
- **In high-risk patients**, EBV viral load monitoring should be performed **weekly during the first 3–4 months, every two weeks until month 6, and then monthly until the end of the first post-transplant year** (V, B).
- In patients at moderate or low risk, if EBV viral load monitoring is performed, it should be carried out monthly until month 6 and then every three months until the end of the first post-transplant year (V, C).
- In children under one year of age, monitoring should follow the same schedule as for moderate- or low-risk patients (V, C).

Traitement préemptif

2- Conduite à tenir

- No consensus exists regarding the threshold for initiating preemptive therapy; however, a level ≥100,000 copies/mL for SOT recipients or an increase of at least threefold (0.5 $\log_{10}$) between two samples, regardless of transplant type, is proposed (IV, C).
- **Before any preemptive therapy, evaluation for PTLD using PET-CT** is recommended (IV, A).
- Preemptive treatment should, whenever possible, **begin with a reduction in immunosuppression** (IV, A).
- The efficacy of preemptive therapy should initially be **monitored on a weekly basis** (IV, B).
- **If immunosuppression reduction is ineffective, rituximab administration is recommended** (III, A).
- Preemptive rituximab therapy consists of a **single intravenous infusion** at 375 mg/m², with a second infusion after one week if the response is insufficient (III, A).
- An EBV viral load <10,000 copies/mL is proposed as the threshold for efficacy (IV, C).
- If two rituximab infusions are ineffective, repeat PET-CT imaging is recommended to assess for PTLD, and evaluation for EBV integration within T lymphocytes may be considered (V, C).
- In cases of confirmed treatment failure or contraindication to rituximab, the use of EBV-specific cytotoxic T lymphocytes (CTLs) should be considered (IV, B).

Traitement préemptif



IS = immunosuppression

Traitement
1- Baisse de l'immunosuppression

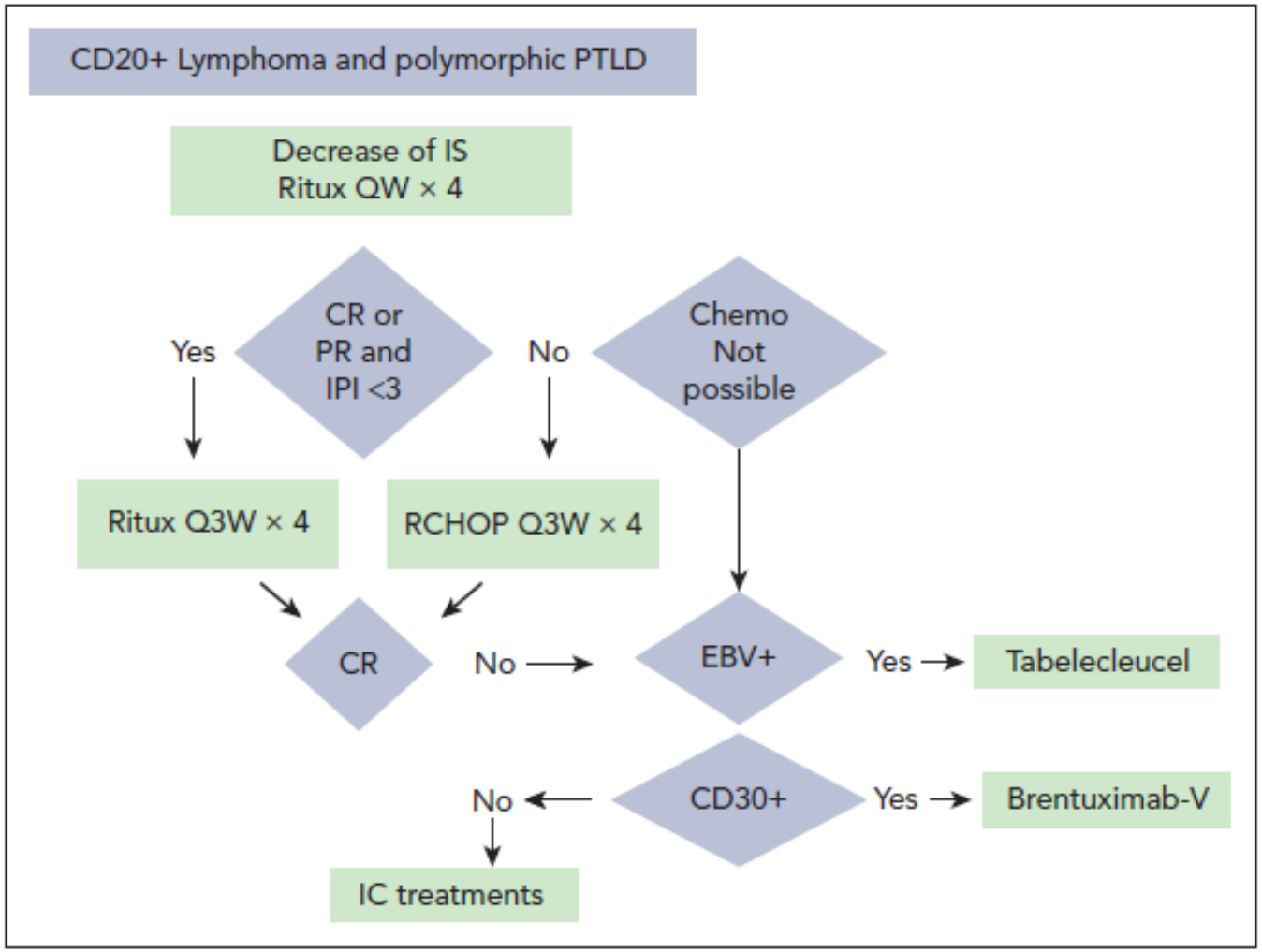
- Management of PTLD **after SOT** should begin, **whenever feasible**, with reduction of immunosuppression (**RIS**). (III, A)
- RIS must be performed **by the transplant team**. (V, A)
- RIS is not **recommended after HSCT**. (IV, B)
- RIS may be used as **sole first-line** therapy **in non-destructive PTLD**, limited **plasmacytoma**-like PTLD, and **EBV-MCU**. (IV, A)
- If RIS is used alone, response assessment is recommended after 4 weeks. (V, C)
- During RIS, **discontinuation of calcineurin inhibitors is not recommended**. (IV, B)
- **Renal graft removal** as a strategy for RIS should be **abandoned**. (V, B)

Traitement
2- LPT CD20+ polymorphique et LNH (monomorphiques)

- CD20+ **polymorphic** PTLD **and NHL-type** PTLD should be **managed identically**. (III, A)
- In adults, **sequential therapy** (ST) **is the standard first-line** treatment for CD20+ polymorphic and NHL-type PTLD **after SOT**. (III, A)
- **After the 4 weekly rituximab** doses of ST, continuation with **rituximab every 21 days ×4 is possible in case of CR and initial IPI <3**. (III, A)
- **In children after SOT**, first-line therapy may consist of **4 weekly rituximab** infusions. (IV, B)
- In children after SOT, in case of CR or PR after rituximab alone, consolidation with rituximab (weekly or every 21 days) is possible but not validated. (IV, C)
- **After HSCT**, first-line therapy consists of **4 weekly rituximab infusions**. (IV, A)
- **ST is not recommended after HSCT**. (IV, A)
- **Second-line** treatment of **EBV+ PTLD** should preferentially be **tabelecleucel**, if available. (III, A)
- **If** PTLD is **CD30+**, **second-line** treatment may include **brentuximab vedotin** (BV), either **alone or in combination**. (III, B)
- **If neither tabelecleucel nor BV** can be used, **chemotherapy** regimens **used in immunocompetent NHL** are recommended. (IV, B)

Traitement

2- LPT CD20+ polymorphique et LNH (monomorphiques)



Choquet S *Blood* 2024

Traitement
3- LPT SNC

- CNS PTLD should, **whenever feasible**, be treated with **high-dose methotrexate**, with or without cytarabine. (IV, B)
- Methotrexate **dose adjustment according to renal function** is an option in CNS PTLD. (IV, C)
- **ST is not recommended** for CNS PTLD. (IV, B)
- In CNS PTLD, rituximab monotherapy, intrathecal chemotherapy, and radiotherapy should be reserved for cases in which methotrexate-based chemotherapy cannot be administered. (IV, C)
- **In relapsed/refractory** CNS PTLD, the standard treatment is **tabelecleucel**, if available, except in rare EBV-negative cases. (IV, B)
- If tabelecleucel is unavailable for relapsed/refractory CNS PTLD, treatments commonly used in immunocompetent patients may be proposed. (IV, C)
- Lenalidomide should be used with caution due to the increased risk of graft rejection. (IV, C)

Traitement

4- Traitements particuliers

- In **localized PTLD**, **surgery or radiotherapy** are **possible** options. (IV, B)

- **CAR-T cells** should, whenever possible, be **reserved for patients in whom immunosuppression can be discontinued or maintained as corticosteroid monotherapy** before lymphocyte collection and for at least 1 month after infusion. (IV, C)

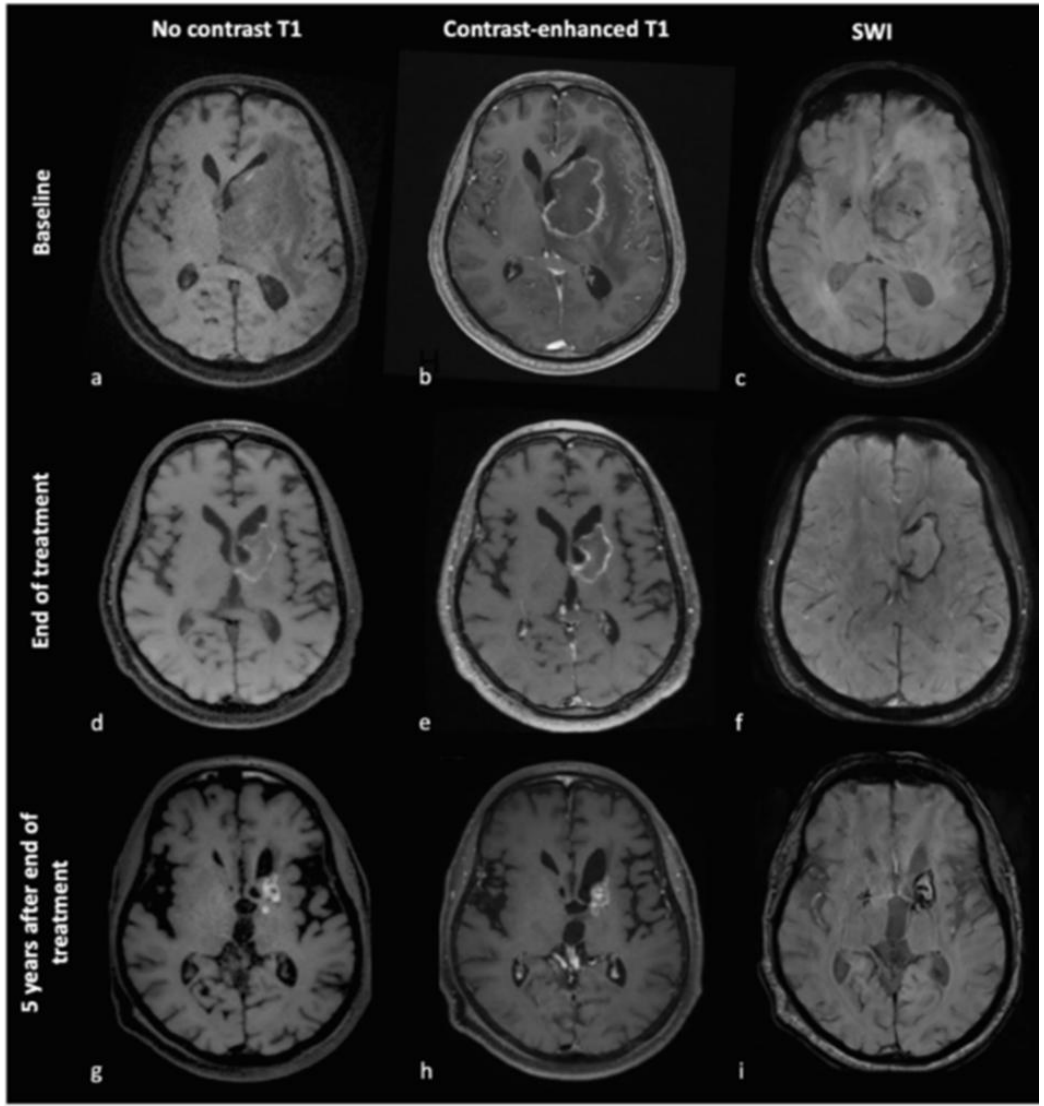
Traitement
5- Autres LPT

- **Relapsed/refractory non-destructive PTLD and EBV-MCU** after RIS should be treated with **weekly rituximab ×4**. (IV, C)
- EBV-negative PTLD in children may be treated with attenuated anthracycline-free chemotherapy (e.g., cyclophosphamide + prednisone + rituximab). (IV, C)
- **T-cell NHL-type** PTLD may include **BV** in the treatment regimen **in CD30+ cases**, starting **from first line**. (IV, C)
- Classical **Hodgkin**-type PTLD should be treated while avoiding intensive regimens; **ABVD or BV-AVD** should be preferred. (IV, C)
- Burkitt-type PTLD may be treated with ST, R-CHOP, or regimens similar to those used in immunocompetent patients. (IV, C)
- Localized plasmacytoma-like PTLD may be treated with RIS alone, surgery, or radiotherapy. (IV, C)
- Relapsed/refractory localized plasmacytoma-like PTLD may be treated with surgery, radiotherapy, or CHOP. (IV, C)
- **Disseminated plasmacytoma-like PTLD** may be treated with agents and **protocols effective in multiple myeloma**. (IV, C)
- There are no specific recommendations for plasmablastic PTLD. Myeloma-type or hybrid myeloma/NHL regimens may be proposed (e.g., daratumumab-CHOP). (V, C)

Surveillance post traitement

- EBV viral load, if elevated at diagnosis, should be monitored during and after treatment. (IV, C)
- EBV viral load alone should not determine a change in therapeutic line. (V, C)
- **Persistently elevated EBV viral load** without decline **should prompt evaluation for treatment failure**. (V, C)
- During long-term follow-up, a **renewed increase in EBV viral load** after completion of therapy should prompt **investigation for relapse** (PET-CT) **and** consideration of **preemptive treatment**. (V, C)
- **For systemic PTLD, PET-CT** is the reference imaging modality for follow-up. (IV, B)
- **For CNS PTLD, MRI** is the reference imaging modality, with **CSF** analysis **in case of lymphomatous meningitis**. (IV, A)
- **MRI response assessment** in CNS PTLD should be performed cautiously and **according to ARCIP criteria**. (IV, A)
- Follow-up schedule may follow each center’s practice for NHL in immunocompetent patients. (V, C)

Critères ARCIP
(Adapted Response Criteria for Immunocompromised PCNSL Patients)



	Proposed ARCIP criteria
CR	Complete disappearance of all enhancing abnormalities on gadolinium-enhanced MRI
CRu	Decrease in size and edema of the overall lesion and enhancement AND Enhancement restricted to a hemorrhagic area evaluated by susceptibility-weighted imaging Repeat MRI at 1 and 3 months after treatment interruption. If stable or decreased: CR
PR	Decrease in size and edema of the overall lesion and enhancement AND Enhancement in a nonhemorrhagic area
SD	Stability in size of the overall lesion and enhancement
PD	Size increase of the lesion and enhancement New enhancing lesion

Abbreviations: CR: Complete Response, CRu: unconfirmed Complete Response, PR: Partial Response, SD: Stable disease

Schulz N et al. *Neurooncol* 2024


MERCI POUR VOTRE ATTENTION!!!!!!
VOUS POUVEZ POSER LES QUESTION MAINTENANT (SI IL Y EN A)