expression varies among patients, with an overall expression rate lower than 50% in one study but not in another [140, 141]. ATL cells frequently express CD52 as compared to other PTCLs. The humanized anti-CD52 monoclonal antibody alemtuzumab is active against CLL and PTCL as a single agent. The combination of alemtuzumab with a standard-dose cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) regimen as a first-line treatment for 24 patients with PTCL showed promising results with CR in 17 (71%) patients, 1 had a partial remission, with an overall median duration of response of 11 months and was associated with mostly manageable infections but including CMV reactivation [142]. Major infections were Jacob–Creutzfeldt virus reactivation, pulmonary invasive aspergillosis, and Staphylococcus sepsis.

ATL cells express CD52, the target of alemtuzumab, which was active in a preclinical model of ATL and toxic to p53-deficient cells, and several ATL cases successfully treated with this agent have been reported [143–145].

Siplizumab is a humanized MoAb targeting CD2 and showed efficacy in a murine ATL model. P1 dose-escalating study of this agent in 22 patients with several kinds of T/NK-cell malignancy revealed six responses (two CR in LGL leukemia, three PR in ATL and one PR in CTCL). However, four patients developed EBV-associated LPD [146]. The broad specificity of this agent may eliminate both CD4- and CD8-positive T cells as well as NK cells without affecting B cells and predispose individuals to the development of EBV lymphoproliferative syndrome.

CCR4 is expressed on normal T helper type 27 and regulatory T (Treg) cells and on certain types of T-cell neoplasms [63, 94]. KW-0761, a next generation humanized anti-CCR4 mAb, with a defucosylated Fc region, exerts strong antibody-dependent cellular cytotoxicity due to increased binding to the Fcγ receptor on effecter cells [147]. A phase I study of dose escalation with four weekly intravenous infusions of KW-0761 in 16 patients with relapsed CCR4-positive T-cell malignancy (13 ATL and 3 PTCL) revealed that one patient, at the maximum dose (1.0 mg/kg), developed grade (G) three dose-limiting toxic effects, namely skin rashes and febrile neutropenia, and G4 neutropenia [148]. Other treatment-related G3-4 toxic effects were lymphopenia ($n=10$), neutropenia ($n=3$), leukopenia ($n=2$), herpes zoster ($n=1$), and acute infusion reaction/cytokine release syndrome ($n=1$). Neither the frequency nor severity of these effects increased with dose escalation or the plasma concentration of the agent. The maximum tolerated dose was not reached. No patients had detectable levels of anti-KW-0761 antibody. Five patients (31%; 95% CI, 11–59%) achieved objective responses: two complete (0.1; 1.0 mg/kg) and three partial (0.01; 2 at 1.0 mg/kg) responses. Three out of thirteen patients with ATL (31%) achieved a response (two CR and one PR). Responses in each lesion were diverse, that is, good in PB (six CR and one PR/seven evaluable cases), intermediate in skin (three CR and one PR/eight evaluable cases), and poor in LN (1 CR and 2 PR/11 evaluable cases). KW-0761 was well tolerated at all the doses tested, demonstrating potential efficacy against relapsed CCR4-positive ATL or PTCL. Recently, results of subsequent phase II studies at the 1.0 mg/kg in relapsed ATL, showing 50% of response rate with acceptable toxicity profiles, were reported [149]. Also, a phase II trial of single agent KW-0761 at the 1.0 mg/kg in relapsed PTCL/CTCL and a phase II trial of VCAP-AMP-VECP combined with KW-0761 for untreated aggressive ATL are ongoing.

Other Novel Agents

Pralatrexate (Folotyn) is a new agent with potent preclinical and clinical activity in T-cell malignancies including ATL [150–152]. The agent is a novel anti-folate with improved membrane transport and polyglutamylation in tumor cells and high affinity for the reduced folate carrier highly expressed in malignant cells. Other potential drugs for ATL under investigation include a proteasome inhibitor, bortezomib (Velcade), and an immunomodulatory agent, lenalidomide (Revlimid) [153–155].

Table 8.3 Strategy for the treatment of Adult T-Cell Leukemia-Lymphoma

Smoldering- or favorable chronic-type ATL
• Consider inclusion in
• Symptomatic patients (skin lesions, opportunistic infections, etc.): Consider AZT/IFN or Watch and Wait
• Asymptomatic patients: Consider Watch and Wait
Unfavorable chronic- or acute-type ATL
• If outside clinical trials, check prognostic factors (including clinical and molecular factors if possible):
– Good prognostic factors: consider chemotherapy (VCAP-AMP-VECP evaluated by a phase III trial against biweekly-CHOP) or AZT/IFN (evaluated by a meta-analysis on retrospective studies)
– Poor prognostic factors: consider chemotherapy followed by conventional or reduced intensity allo-HSCT (evaluated by retrospective and prospective Japanese analyses, respectively).
– Poor response to initial therapy: Consider conventional or reduced intensity allo-HSCT
Lymphoma-type ATL
• If outside clinical trials, consider chemotherapy (VCAP-AMP-VECP)
• Check prognostic factors (including clinical and molecular factors if possible) and response to chemotherapy:
– Good prognostic factors and good response to initial therapy: Consider chemotherapy followed by observation
– Poor prognostic factors or poor response to initial therapy: Consider chemotherapy followed by conventional or reduced intensity allo-HSCT

[Based on data from Tsukasaki K, Hermine O, Bazarbachi A, et al.: Definition, prognostic factors, treatment, and response criteria of adult T-cell leukemia-lymphoma: A proposal from an international consensus meeting. J Clin Oncol 27:453–459, 2009.]

Prevention of ATL

Two steps should be considered for the prevention of HTLV-1-associated ATL. The first is the prevention of HTLV-1 infections. This has been achieved in some endemic areas in Japan by screening for HTLV-1 among blood donors and asking mothers who are carriers to refrain from breast feeding. The second step is the prevention of ATL among HTLV-1 carriers. This has not been achieved partly because only about 5% of HTLV-1 carriers develop the disease in their life time, although several risk factors have been identified by a cohort study of HTLV-1 carriers (Joint Study of Predisposing Factors for ATL Development) [83]. Also, no agent has been found to be effective in preventing the development of ATL among HTLV-1 carriers.

Ongoing Clinical Trials

Clinical trials have been paramount to the recent advances in ATL treatment, including assessments of chemotherapy, AZT/IFN, and allo-HSCT. Recently, a strategy for ATL treatment, stratified by subclassification, prognostic factors, and the response to initial treatment as well as response criteria was proposed (Table 8.3) [57]. The recommended treatment algorithm for ATL is shown in Fig. 8.2. However, as described in this chapter, ATL still has a worse prognosis than the other T-cell malignancies [156]. There is no plateau with an initial steep slope and subsequent gentle slope without a plateau in the survival curve for aggressive or indolent ATL treated by watchful waiting and with chemotherapy, respectively, although the prognosis is much better in the latter [14, 61]. A prognostic model for each subgroup should be elucidated to properly identify the candidate for allo-HSCT which can achieve a cure of ATL despite considerable treatment-related mortality. Although several small phase II trials suggested IFN/AZT therapy to be promising, no confirmative phase III study has been conducted. Furthermore, as described in the other chapters in detail, more than ten promising new agents for PTCL/CTCL including ATL are now in clinical trials or preparation. Future clinical trials on ATL as described above should be incorporated to ensure that the strategy as shown in Table 8.3 is continually updated to establish evidence-based practical guidelines.

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8 成人T細胞白血病・リンパ腫 (adult T-cell leukemia-lymphoma : ATL)

◆ 総論

成人T細胞白血病・リンパ腫（adult T-cell leukemia-lymphoma：ATL）は，九州・沖縄地方を主とする西南日本に多発するT細胞腫瘍として，1977年内山，高月らによって提唱された疾患概念である[1]。1980年代のはじめには原因ウイルスとしてhuman T-lymphotropic virus type-I（HTLV-1）が発見された[2)~5)]。WHO分類（2008）においてATLは，高度の核異型を伴ったリンパ球よりなる，HTLV-1によって引き起こされる末梢性T細胞腫瘍と定義されている[6]。

Flower cellと呼ばれる異常リンパ球の増多を主体とした白血球増多，リンパ節腫脹，皮膚病変，ATL細胞の浸潤による多臓器障害，高LDH血症，高Ca血症，日和見感染症などが出現する。日本以外では中央アフリカおよび中南米出身者に比較的高頻度に発生している。HTLV-1キャリアは現在日本には西南日本沿岸部を主に110万人程度存在し，キャリアからATLの発症率は年間1,000人に0.6~0.7人とされる[7)8)]。HTLV-1の感染は感染細胞が正常リンパ球に直接接触して成立する。感染経路として輸血，性交，母乳が知られているが，ATL発症につながる重要な感染経路は母乳である。いくつかの多発地域ではHTLV-1母子感染予防対策が行われており，6カ月以上の長期授乳による母子感染率は20.5%であるのに対して人工栄養による母子感染率は2.4%と報告されている[9]。

ATL発症は20歳代までは極めて稀で，その後増加し，60歳頃をピークにして以降徐々に減少する。1人のHTLV-1キャリアが，生涯でATLを発症する確率は約5%である。HTLV-1キャリアにおけるATL発症の危険因子としては，多変量解析で，母子感染，高齢者，末梢血中の高ウイルス量，ATLの家族歴あり，他の疾患の治療中に初めて抗HTLV-1抗体検査を受け陽性が判明した症例[10]が報告されている。近年，HTLV-1キャリアとATL患者の高齢化が進んでいる[11)12)]。

1991年にJapan Clinical Oncology Group（JCOG）リンパ腫グループ（LSG）による813例のATL患者の全国実態調査をもとに，多変量解析による予後因子として，年齢，全身状態（performance status：PS），総病変数，高Ca血症，高LDH血症が同定された[13)~16)]。そして予後因子解析と臨床病態の特徴から「急性型」，「リンパ腫型」，「慢性型」，「くすぶり型」の4臨床病型分類が提唱されている[17]（表1）。これらの割合は急性型57%，リンパ腫型24%，慢性型19%，くすぶり型6%であった。急性型，リンパ腫型，予後不良因子（LDH，アルブミン，BUNのいずれか1つ以上が異常値）を持つ慢性型ATLは急速な経過をたどることがほとんどであり，それぞれの生存期間中央値（MST）は6カ月，10カ月，15カ月であることから一括してアグレッシブATLと呼ばれる。一方くすぶり型および予後不良因子を有していない慢性型ATLは比較的緩徐な経過を辿り，それぞれの4年生存割合は約63%と約70%である[18]ことから，インドレントATLと呼ばれる。

JCOG-LSGがアグレッシブATLを対象とし，継続して臨床試験を行ってきたことから，化学療法における反応性の評価では，JCOG治療効果判定規準が広く使用されてきた[14)19)]。近年では非ホジキンリンパ腫と慢性リンパ性白血病に対するもの[20)21)]をもとに改変した修正版ATLに対するJCOG治療効果判定規準[22]が用いられている（表2）。

表 1　ATL 臨床病型の診断規準（文献 17）を改変）

評価項目		くすぶり型	慢性型*1	リンパ腫型*1	急性型*1
抗 HTLV-1 抗体*2		＋	＋	＋	＋
リンパ球数（×10^3/mm^3）*3		＜4	≧4	＜4	
異常リンパ球数*4		≧5%*7	＋*8	≦1%	＋*8
Flower cell		*5	*5	no	＋
LDH		≦1.5N	≦2N		
補正 Ca 値（mg/dL）*6		＜11.0	＜11.0		
組織学的に腫瘍病変が確認されたリンパ節腫大		No		＋	
腫瘍病変	皮膚	*7			
	肺	*7			
	リンパ節	no		yes	
	肝腫大	no			
	脾腫大	no			
	中枢神経	no	no		
	骨	no	no		
	胸水	no	no		
	腹水	no	no		
	消化管	no	no		

空欄は他の病型で規定される条件以外の制約はないことを示す。
N：正常値上限
*1 予後不良因子を有する慢性型：BUN＞施設基準値上限，LDH＞施設基準値上限，血清アルブミン＜施設基準値下限の 1 つでも満たす場合
*2 PA 法あるいは ELISA 法や Western blot 法のいずれかで陽性であること。
Immunofluorescence 法や Western blot 法により，陽性反応が確認されていることが望ましい。測定可能な施設では，Southern blot 法により，HTLV-1 provirus の ATL 細胞への組み込みを確認する。
*3 正常リンパ球と異常リンパ球を含むリンパ球様細胞の実数の和
*4 形態学的に明らかな ATL 細胞
*5 ATL に特徴的な flower cell が認められてもよい。
*6 補正 Ca 値は以下の式で求める。
血清アルブミン値≧4.0(g/dL)の場合：補正カルシウム値(mg/dL)＝総カルシウム値(mg/dL)
血清アルブミン値＜4.0(g/dL)の場合：補正カルシウム値(mg/dL)＝総カルシウム値(mg/dL)－0.8［アルブミン(g/dL)－4］
*7 末梢血中の異常リンパ球が 5%未満でくすぶり型と診断されるには，皮膚あるいは肺に組織学的に腫瘍病変が確認されることが必要である。
*8 末梢血中の異常リンパ球が 5%未満で慢性型または急性型と診断されるには，組織学的に腫瘍病変が確認されることが必要である。

表2 JCOG版ATLに対する治療効果判定規準[22]

【ベースラインで標的病変が存在する場合】

総合効果	評価項目							
	標的病変		非標的病変		骨髄浸潤	末梢血病変（異常リンパ球）	皮膚病変	新病変
	節性	節外性	節性	節外性				
CR	正常	消失	正常	消失	陰性	正常	正常	なし
PR	SPDの50%以上の縮小		正常 or 非増大	消失 or 非増大	問わない（未検可）	正常 or 減少	正常 or 縮小	なし
SD	CR，PR，PDのいずれにも判定されない							
PD	以下のいずれか1項目でも満たした場合にPDと判定する							
	SPDの50%以上の増大 or 節性標的病変の再腫大 or 節外性標的病変の再出現		増大 or 再腫大	増大 or 再出現	陽性化	増加	増大 or 再出現	あり

上記の項目のいずれかでも評価不能であれば総合評価は「評価不能 not evaluable（NE）」とする。

【ベースラインで標的病変が存在しない場合】

総合効果	評価項目					
	非標的病変		骨髄浸潤	末梢血病変（異常リンパ球）	皮膚病変	新病変
	節性	節外性				
CR	正常	消失	陰性	正常	正常	なし
PR*	正常 or 非増大	消失 or 非増大	問わない（未検可）	正常 or 減少	正常 or 縮小	なし
SD	CR，PR，PDのいずれにも判定されない					
PD	以下のいずれか1項目でも満たした場合にPDと判定する					
	増大 or 再腫大	増大 or 再出現	陽性化	増加	増大 or 再出現	あり

上記の項目のいずれかでも評価不能であれば総合評価は「評価不能 not evaluable（NE）」とする。
*CRの規準を満たす場合，総合効果はCRとする。

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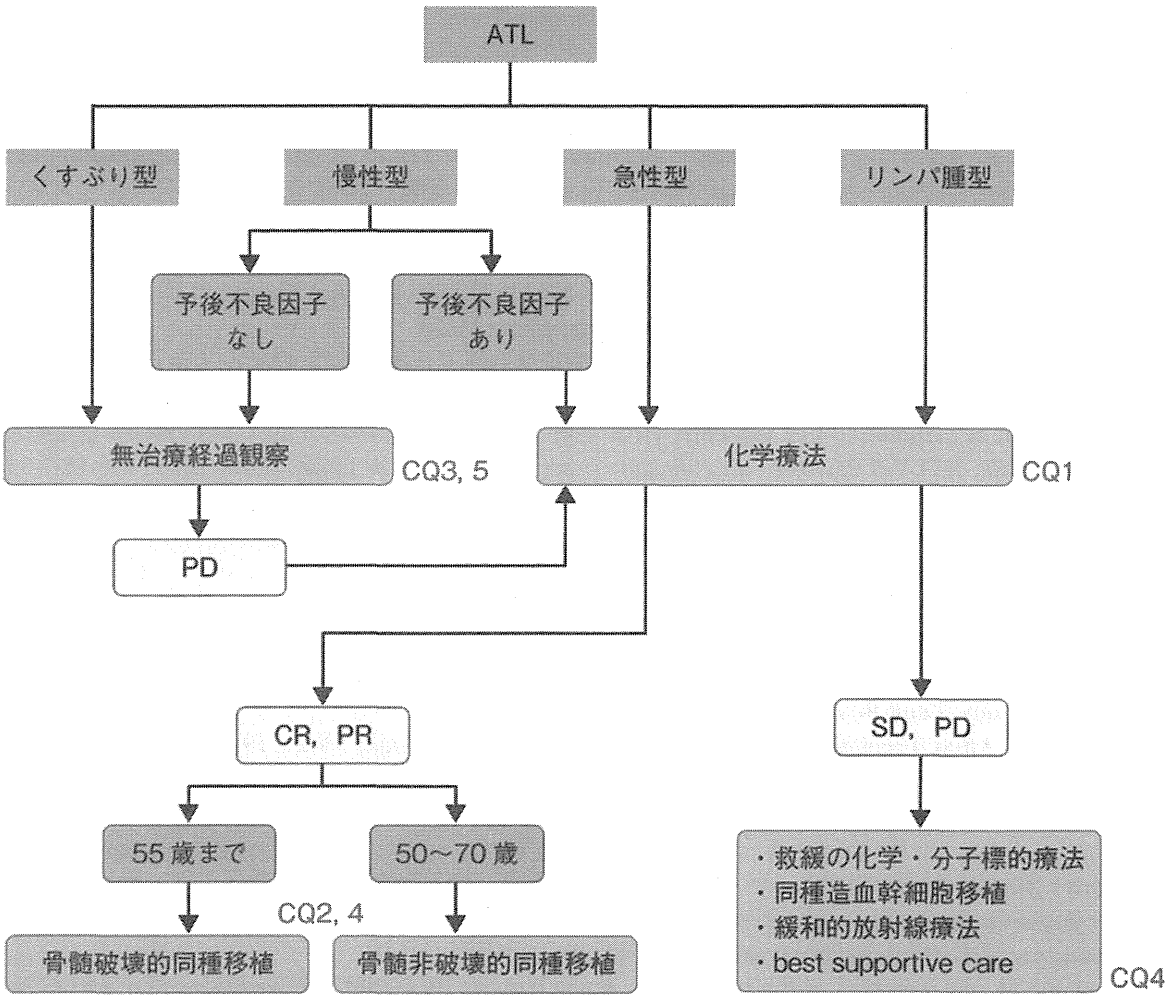
◆ アルゴリズム



急性型，リンパ腫型，予後不良因子（LDH，アルブミン，BUN いずれか一つ以上が異常値）をもつ慢性型，すなわちアグレッシブ ATL に対しては多剤併用化学療法を施行する（CQ1）。そして治療反応性が得られ，年齢・全身状態・主要臓器機能に問題がなく，適切なドナーが見つかった場合は同種造血幹細胞移植（allogeneic hematopoietic stem cell transplantation：allo-HSCT，同種移植）を検討する（CQ2, CQ4）。

くすぶり型，予後不良因子を有していない慢性型，すなわちインドレント ATL に対してはアグレッシブ ATL へ進展するまで無治療経過観察する（CQ3, CQ5）。増悪した後は初発のアグレッシブ ATL と同様に治療する。

CQ 1 初発アグレッシブ ATL に対して最も推奨される治療法は何か

推奨グレード
カテゴリー 1

VCAP-AMP-VECP 療法が最も推奨される。

解 説

1970 年代から 1980 年代にかけて，JCOG-LSG による臨床試験では ATL に対し非ホジキンリンパ腫と同様の化学療法が行われ，その MST は約 8 ヵ月と極めて予後不良であった[1)~3)]。1991 年 JCOG-LSG より ATL の臨床病型分類が提唱された後，アグレッシブ ATL を対象とした臨床試験が継続的に行われてきた。まず 1991 年から，単剤で再発・再燃 ATL に対して治療反応性がみられた[4)] ペントスタチンを組み入れた化学療法の第Ⅱ相試験が行われたが，従来の治療成績を上回らなかった[5)]。1994 年から行われた 8 つの抗がん剤を用い，G-CSF を用いて治療強度を高め，メトトレキサート（MTX）とプレドニゾロン（PSL）の髄注を併用した LSG15 療法の第Ⅱ相試験では，それまでの ATL の治療成績と比較して良好な成績が得られた[6)]。そして 1998 年から VCAP（VCR, CPA, DXR, PSL）-AMP（DXR, MCNU, PSL）-VECP（VDS, ETP, CBDCA, PSL）（modified LSG15）療法と，非ホジキンリンパ腫の標準治療の一つと当時みなされていた CHOP-14 療法とを比較する第Ⅲ相試験（JCOG9801）が行われ，VCAP-AMP-VECP 療法は血液毒性は高いものの CHOP-14 療法よりも完全奏効割合と全生存割合に優れており，ATL に対する標準治療と考えられる[7)]。ただ，この臨床試験は 70 歳未満を対象としたため，高齢者への適用の可能性に関しては不明である。

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CQ 2 アグレッシブATLに対する同種造血幹細胞移植は有用か

推奨グレード
カテゴリー2A

ATLに対する初回治療に反応性がみられた症例に対しては，HLA一致血縁，非血縁ドナーが得られた場合，同種造血幹細胞移植は長期生存が期待できる治療法として推奨される。

解 説

ATLに対する同種造血幹細胞移植（allogeneic hematopoietic stem cell transplantation：allo-HSCT）は，自家造血幹細胞移植併用大量化学療法では再発が極めて高率であるのに対し，当初単施設からの少数例の報告で化学療法では得難い長期生存例が確認された。その後に多施設後方視的解析の結果から，1年全生存割合（OS）50～52%，3年OSが45%と有望な成績が報告された[1)~4)]。そして大規模な後方視的調査として日本のデータベースを基に，allo-HSCTが施行されたATL 386例の3年OSが33%と報告された[5)]。

これらはallo-HSCTを施行し得たという選択された一群に対してではあるが，化学療法単独と比較して有望な治療成績である。移植片対宿主病（graft-versus-host disease：GVHD）合併症例において再発率が低いこと，移植後再発例において免疫抑制剤の減量・中止により再寛解に到達した症例があることなどから，移植片対ATL（graft-versus-ATL：GvATL）効果が有望な治療成績の要因の一つと考えられる。ATLに対する初回治療後に治療反応性がみられた症例には，HLA一致血縁ドナー，非血縁ドナーが得られた場合，allo-HSCTは長期生存，さらには治癒が期待できる治療法として推奨される。ただしいずれの報告でもGVHD，感染症などによる高い治療関連死亡（TRM）が示されており，化学療法後に長期奏効が得られる場合も稀にはあるため，患者へは十分な情報の提供が必要である。

allo-HSCTで骨髄破壊的前処置もしくは骨髄非破壊的前処置のいずれを選択するかについて明確なデータはないが，年齢で分けることが一般的である。骨髄破壊的前処置の対象年齢の上限は55歳，そして骨髄非破壊的前処置は50～70歳（非血縁の場合は65歳まで）を対象とすることが実臨床と臨床試験では行われている[6)~8)]。近年，血縁HTLV-1キャリアドナーからのallo-HSCT施行後に，ドナーHTLV-1感染細胞由来の再発例が報告された[9)]。その後，日本造血細胞移植学会から，血縁キャリアをドナーとする場合には末梢血を用いたHTLV-1のサザンブロット解析でモノクローナル/オリゴクローナルでないこと，臨床的にATLくすぶり型でなくHTLV-1キャリアに留まることを確認することが推奨されている[10)]。

ATLに対するallo-HSCTは，化学療法では得難い長期生存例が観察されており有効な治療法と言える。しかし，ドナーの選択，前処置法，高い移植関連死亡を減少させる感染症予防の方法などコンセンサスが得られていない課題も多い。現在日本で，アグレッシブATLに対するallo-HSCTの臨床試験が進行中である。

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CQ 3 インドレント（くすぶり型，予後不良因子を持たない慢性型）ATLの標準治療は無治療経過観察か

推奨グレード
カテゴリー2B

インドレントATLに対する化学療法は生存期間の延長にはつながらず，無治療経過観察が推奨される。

解　説

九州および沖縄の40施設におけるくすぶり型および慢性型ATL 337例を対象とした後方視的解析では[1]，その生存期間中央値（MST）はそれぞれ5.2年と3.6年であった。そのサブグループ解析では，くすぶり型での無治療群と抗がん剤投与群との間で全生存期間（OS）に差はなかった。一方，慢性型では無治療群の方が抗がん剤投与群よりも有意に生存期間が長かった（MST 7.4年 vs 2.0年）。また，1988～1997年に九州の多施設でくすぶり型ATLと診断された26例のMSTは7.3年（観察期間中央値6.5年）であった[2]。また，単施設での後方視的研究報告によると，1974～2003年にくすぶり型（25例），慢性型（予後不良因子を持つ慢性型37例，予後不良因子を持たない慢性型26例，不明2例）と診断され，増悪するまで無治療経過観察が行われた計90例では，観察期間中央値が4.1年の時点で12人が10年以上生存していた。しかし，2年，5年，10年，15年生存割合はそれぞれ約60%，47%，23%，13%と長期予後は不良であった[3]。MSTと無増悪MSTはそれぞれ4.1年と3.3年であり，くすぶり型と慢性型の生存曲線がいずれもプラトーに到達せず下降したことから，増悪後のMSTは約1年と推定され，MSTは長く長期生存例が一定の割合で存在するものの，増悪後の予後は不良であることが示唆される。

以上のようにインドレントATLの長期予後は決して良好ではない。しかし，有効な治療法がまだ見出されていないため，急性転化まで無治療で経過観察することが，わが国では現在コンセンサスとして定着している。

くすぶり型で皮膚病変のみを持つ症例の局所治療は，皮膚悪性腫瘍診療ガイドライン[4]の参照が推奨される。

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CQ 4 再発・難治アグレッシブ ATL に対する治療法は何が勧められるか

推奨グレード
カテゴリー 2B

現時点で同種造血幹細胞移植が生存に寄与する唯一の救援療法である。モガムリズマブの有用性については現在評価中である。

解　説

アグレッシブ ATL に対してはこれまでさまざまな化学療法が試みられてきたが，一旦治療効果が得られてもその持続期間は短く，その後は急速な経過を辿ることが多い。そのため臨床試験の遂行は困難で，単施設での少数例の報告がほとんどである。わが国における modified EPOCH 療法（ETP, DXR, CPA, VCR, PSL）[1]，ペントスタチン [2]，ソブゾキサン [3]，塩酸イリノテカンとシスプラチン併用 [4] などの小規模な第Ⅰ・Ⅱ相試験の結果が報告されている。いずれも奏効割合は 30～40％であったが，効果持続期間は 1～6 ヵ月であった。

ケモカイン受容体の CCR4 は ATL の 90％以上で発現しており，予後不良因子でもある。ヒト化抗 CCR4 抗体（モガムリズマブ）の第Ⅰ相試験では再発難治のアグレッシブ ATL 13 名中 4 名に治療反応がみられ [5]，さらには至適投与量の単剤での第Ⅱ相試験で 13/26 名（50％，うち 8 名は CR）に奏効したことが報告された [6]。2012 年 5 月よりモガムリズマブは再発・難治性 ATL に対して承認された。現在，初発のアグレッシブ ATL を対象としたモガムリズマブと VCAP-AMP-VECP 療法［VCAP（VCR, CPA, DXR, PSL），AMP（DXR, MCNU, PSL），VECP（VDS, ETP, CBDCA, PSL）］との併用療法のランダム化第Ⅱ相比較試験が進行中であり，今後の評価が必要である。

CQ2 にあるように，同種造血幹細胞移植（allogeneic hematopoietic stem cell transplantation：allo-HSCT）は化学療法後の再発・難治アグレッシブ ATL の一部に長期生存をもたらすことが複数の報告で示されている。

局所再発の場合，症状緩和を目的とした局所放射線療法を行ってもよい [7]。

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CQ 5 ATLに対するインターフェロンαとジドブジンの併用療法は有用か

推奨グレード
カテゴリー3

ATLに対するインターフェロンα/ジドブジン療法は，一般診療としては推奨されない。

解説

ATLはCHOP療法などのリンパ腫に対する標準治療では難治であり，HTLV-1が関与することから，欧米ではインターフェロンα（IFNα）とジドブジン（AZT）の併用療法が検討され，1995年には2つの小規模な臨床試験でアグレッシブATLに対する有望な奏効割合が報じられた[1)2)]。しかし，初発例に限るとその奏効割合と生存期間中央値（MST）は当時のJCOG-LSGによる化学療法より下回っていたこともあって，日本でこの治療法は本格的に検討されなかった[1)~3)]。2010年に，欧州と北中南米での後方視的併合解析において，リンパ腫型よりも白血化している急性型，慢性型，くすぶり型で本治療法が有用であったと報告された[4)]。これを受けてNCCNガイドラインでは，リンパ腫型以外のATLに対してIFNα/AZT療法を推奨している（NCCNガイドライン：カテゴリー2A）。またこの報告では，IFNα/AZT療法群での治療成績は白血化しているこれらの3病型で化学療法群を上回っていた一方，急性型ATLに対する化学療法の治療成績は，日本での化学療法の成績を下回っていた。一方，慢性型とくすぶり型では，症例数は少ないものの観察期間中央値5年で全例が生存しており，皮膚病変の改善にも有用と報告された[4)]。本併用療法は，長期にわたる治療が必要であり，倦怠感などの全身症状，造血障害など多様な有害事象を認めるものの，化学療法や同種造血幹細胞移植（allogeneic hematopoietic stem cell transplantation：allo-HSCT）に比べて毒性は低いと報告されている。

以上よりIFNα/AZT療法は，確かにATLに対して有望な治療法であるが，これまでの海外での小規模な臨床的検討と後方視的解析によるエビデンスが十分でないことから，一般診療では推奨されない。なお，IFNα，AZTともにATLでは国内適応外である。現在わが国で，インドレントATLに対するIFNα/AZT療法と無治療経過観察との比較試験が計画されている。

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