9th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

Infections in AML and ALL patients treated with new molecules and antibodies

▶ VIRTUAL CONFERENCE
From September
16th to 17th 2021

Final revised slide set post-ECIL meeting

Infectious Complications of Targeted Drugs and Biotherapies in Acute Leukemia

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Agents Included

- Inotuzumab ozogamicin (CD22; ALL): Garcia-Vidal, Maschmeyer
- Gemtuzumab ozogamicin (CD33; AML): Maschmeyer, Garcia-Vidal
- Flotetuzumab (CD3xCD123; AML): Maschmeyer, Garcia-Vidal
- Ivosidenib and Enasidenib (IDH-1 and -2; AML): Thiebaut, Herbrecht
- Gilteritinib (FLT3; AML): Maertens, Thiebaut
- Midostaurin (FLT3; AML): Pagano, Calandra
- Quizartinib (FLT3; AML): Pagano, Maertens
- Glasdegib (Hedgehog; AML): Bullinger, Herbrecht
- Venetoclax (BCL-2; AML): Bullinger, Herbrecht
- Drug interactions: Menna

Drug Approval status

- Divide the paper to separately address approved vs non-approved (but available somewhere) drugs

- Flotetuzumab
- Quizartinib
- Enasidenib

Grading System

Strength of a recommendation		
Grade A	ECIL	strongly supports a recommendation for use
Grade B		moderately supports a recommendation for use
Grade C		marginally supports a recommendation for use
Grade D		supports a recommendation against use
Quality of Evidence		
Level I		Evidence from at least one properly designed randomized, controlled trial
Level II*		Evidence from at least one well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 centre); from multiple time series; or from dramatic results of uncontrolled experiments
Level III		Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies, or reports of expert committees

*Added index:

$_r$: Meta-analysis or systematic review of randomized controlled trials.

$_t$: Transferred evidence, that is, results from different patients' cohorts, or similar immune-status situation.

$_h$: Comparator group is a historical control.

$_u$: Uncontrolled trial.

$_a$: Published abstract (presented at an international symposium or meeting).

Inotuzumab ozogamicin

Recommendations for prophylaxis/Recommendations on how to handle the drug in case of infection

- This drug does not increase the risk of infection
- No specific prophylaxis is needed (A-IIr)
- No specific recommendation with the use of this drug are needed in case of infection Special attention when combining this drug with other agents prolonging QT interval (A-IIr)

Gemtuzumab ozogamicin

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-IIr)

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- Standard of care in AML, when given in combination (A-IIr) or high-dose GO for relapse (A-IIr)
- No systemic prophylaxis when given as monotherapy (A-IIr)

Recommendations on how to handle the drug in case of infection:

- Most infections after GO application, so no recommendation

General recommendation

- Careful monitoring of hepatotoxicity (A-I)

Flotetuzumab (MGD006)

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-IIr)

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- No specific recommendation due to lack of data when given as monotherapy

Recommendations on how to handle the drug in case of infection:

- No specific recommendation due to lack of data when given as monotherapy

Ivosidenib or Enasidenib (IDH1 and 2 inhibitors)

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-II)
  - In combination with more intensive antileukemic treatment, Clostridia infections were reported from single center

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- No systemic prophylaxis when given as monotherapy (A-IIr)

Recommendations on how to handle the drug in case of infection:

- No specific recommendations

Gilteritinib

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-IIr)

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- No systemic prophylaxis when given as monotherapy (A-IIr)

Recommendations on how to handle the drug in case of infection:

- No specific recommendations

Midostaurin (FLT3 inhibitor AML)

Recommended diagnostic procedures (differential diagnoses):

- Microbiological work-up for fever during 3+7 plus midostaurin therapy (A-IIr)

Treatment recommendations:

- Use of empirical antibiotic approach during 3+7 plus midostaurin therapy in neutropenic fever and/or infections (A-IIr)

Recommendations for antibiotic prophylaxis:

- Standard of care when midostaurin is given in combination with 3+7 (A-IIr) or as monotherapy (C-III)

Recommendations for antifungal prophylaxis:

- No evidence that midostaurin can cause an IFI increase
- Warning of midostaurin-azole D-D interaction (no use of triazoles, itra/keto/posa/vori = package insert) during midostaurin administration.

Quizartinib

Recommended diagnostic procedures (differential diagnoses):

- Microbiological work-up for fever during therapy (A-IIr)

Treatment recommendations:

- Use of empirical antibiotic approach in neutropenic fever and/or infections (A-IIr)

Recommendations for antibiotic prophylaxis:

- Standard of care in AML, when given in combination (A-IIr)

Glasdegib

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-IIr)

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- Standard of care in AML, when given in combination (A-IIr)

Recommendations on how to handle the drug in case of infection:

- No specific recommendations

Venetoclax

Recommended diagnostic procedures (differential diagnoses):

- Standard of care in AML and neutropenic fever and/or infections (A-IIr)

Treatment recommendations:

- Standard of care in neutropenic fever and/or infections (A-IIr)

Recommendations for prophylaxis:

- Standard of care in line with AML treatment with intensive chemotherapy, as combination of venetoclax and HMA has similar neutropenia / neutropenic fever / infection rates (A-IIr)
- Posaconazole + venetoclax: reduction of venetoclax by 75% (A-I)

Venetoclax

Further recommendations for prophylaxis:

- In contrast to current guidelines on antibacterial prophylaxis in HMA recipients, consider AB proph when HMA are combined with venetoclax (A-IIr)
- Same for systemic antifungal prophylaxis (A-IIr)
- Ensure proper venetoclax dose adjustments when venetoclax is combined antibacterials such as ciprofloxacin or macrolides (A-I)

Venetoclax

Recommendations on how to handle the drug in case of infection:

- Consider dose interruptions to allow for hematologic recovery in patients with a response (based on early bone marrow assessment, most importantly after the completion of cycle 1) (A-I)
- Promote appropriate application of interruptions in venetoclax between treatment cycles to augment hematologic recovery (A-I)
- In pts with good response but severe neutropenia, consider venetoclax dose reduction in subsequent courses (A-IIr)
- If dose reduction is ineffective or not advised, consider prophylactic granulocyte colony-stimulating factor during remission for subsequent courses (C-IIt)