MZL endpoints & emerging prognostic markers

The main objective of this survey among experts is to draw up a list of potential prognostic markers for PFS in MZL trials. Thereafter, these proposals will serve as a basis to perform the assessment of prognostic value of emerging prognostic markers in MZL by a meta-analysis on aggregated IPD data.

This questionnaire is divided in 4 parts:
- Respondents' characteristics
- Emerging prognostic markers at baseline
- Emerging prognostic markers assessed during follow-up
- Endpoints definitions

Thanks a lot !
Côme Bommier, Jérôme Lambert & Catherine Thieblemont

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This questionnaire is divided in 4 parts:
A- Respondents' characteristics
B- Emerging prognostic markers at baseline
C- Emerging prognostic markers assessed during follow-up
D- Endpoints definitions

Thanks a lot !
Côme Bommier, Jérôme Lambert & Catherine Thieblemont

Part A. Q1.

What is your sex ?

◯ Female
◯ Male

Part A. Q2.

What is the year of your birth ?

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Part A. Q3.

What is your main speciality ?

◯ Clinical hematology (ward)
◯ Biological hematology (lab)
◯ Radiology or Nuclear medicine
◯ Pathology
◯ Biostatistics or Epidemiology
◯ Other

What is your speciality ?

_____

Part A. Q4.

Have you already participated in a TRIAL involving ONLY MZL patients?

- ☐ Yes, as primary investigator
- ☐ Yes, as coinvestigator
- ☐ Yes, as methodologist
- ☐ Yes, as member of the trial management group (responsible for the day-to-day delivery and conduct of the trial)
- ☐ Yes, as member of the executive trial steering committee (experienced and independent experts aiming at quality assurance of the trial and patient advocacy)
- ☐ Yes, as member of the data monitoring committee (role is to review safety and efficacy data and make recommendations to an executive group)
- ☐ No, I have never taken part in such trial

Part A. Q5.

Have you already participated in a TRIAL involving MZL patients, merged with other lymphomas patients (such as FL patients)?

- ☐ Yes, as primary investigator
- ☐ Yes, as coinvestigator
- ☐ Yes, as methodologist
- ☐ Yes, as member of the trial management group (responsible for the day-to-day delivery and conduct of the trial)
- ☐ Yes, as member of the executive trial steering committee (experienced and independent experts aiming at quality assurance of the trial and patient advocacy)
- ☐ Yes, as member of the data monitoring committee (role is to review safety and efficacy data and make recommendations to an executive group)
- ☐ No, I have never taken part in such trial

Part A. Q6.

Have you already authored a COHORT including MZL patients ?

- ◯ Yes (first author or any co-author)
- ◯ No

Part B. Emerging prognostic markers at baseline in MZL trial

At the time of the questionnaire, prognostic tools are MALT-IPI score (Thieblemont, 2017), HPLL score (Montalban, 2014) and ILL score (Arcaini, 2006).
Let suppose you are designing a NEW TRIAL with UNLIMITED possibilities...

Part B. Q1.

Among markers at BASELINE, what is(are) the EMERGING markers you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ PET-CT at baseline
- ☐ cfDNA at baseline
- ☐ Cytogenetics
- ☐ Molecular tumor variants by NGS
- ☐ Other

You ticked "Other". So among markers at BASELINE, what is the EMERGING markers you think worthwhile to be evaluated as prognostic for PFS in MZL ?

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Part B. Q2.

Among PET-CT measures at baseline, what is(are) the one(those) you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ Total metabolic tumor volume (TMTV) at baseline
- ☐ Deauville score at baseline (Song &al, Sci Reports 2020)
- ☐ SUVmax of the main lesion
- ☐ Any measurement
- ☐ Other
- ☐ I think PET-CT at baseline is not relevant as prognostic marker in MZL

You ticked "Other". So among PET-CT measures AT BASELINE, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

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Part B. Q3.

Among these cytogenetics features at baseline, what is(are) the one(those) you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ del(17p)
- ☐ t(11;18) BIRC3-MALT1
- ☐ t(14;18) IGH-MALT1
- ☐ t(1;14) BCL10-IGH
- ☐ +3
- ☐ +18
- ☐ 6q23-
- ☐ del(7q)
- ☐ Any of them
- ☐ Other
- ☐ I think cytogenetics is not relevant as prognostic marker in MZL

You ticked "Other". So among cytogenetics features AT BASELINE, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

_____

Part B. Q4.

Among these molecular variants at baseline, what is(are) the one(those) you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ TP53
- ☐ NOTCH2
- ☐ KLF2
- ☐ TNFAIP3
- ☐ PTPRD
- ☐ KMT2D
- ☐ Other
- ☐ I think NGS is not relevant as prognostic tool in MZL

You ticked "Other". So among molecular variants AT BASELINE, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

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Part C. Emerging prognostic markers assessed during follow-up in MZL trial

At the time of the questionnaire, response to treatment in MZL is assessed by CT-scan (Cheson, 2014), blood tests (Matutes, 2008) and/or pathology (Copie-Bergmann, 2003). Let suppose you are designing a NEW TRIAL with UNLIMITED possibilities...

Part C. Q1.

Among markers assessed DURING FOLLOW-UP, what is(are) the EMERGING marker you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ PET-CT response assessment
- ☐ cfDNA during follow-up
- ☐ Minimal residual disease (MRD)
- ☐ Other

You ticked "Other". So among markers assessed DURING FOLLOW-UP, what is the EMERGING marker you think worthwhile to be evaluated as prognostic for PFS in MZL ?

_____

Part C. Q2-1.

Among PET-CT measures during follow-up, what is(are) the one(those) you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ SUVmax
- ☐ delta-SUVmax
- ☐ Deauville score
- ☐ Total metabolic tumor volume (TMTV)
- ☐ delta-TMTV
- ☐ Any of them
- ☐ Other
- ☐ I think PET-CT during follow-up is not relevant in MZL

You ticked "Other". So among PET-CT measures DURING FOLLOW-UP, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

_____

Part C. Q2-2.

In a prognostic prospect, at what time from treatment start (in months) do you think it would be relevant to perform PET-CT ?

_____
(Please give a number IN MONTHS (e.g. write M2 if you mean 2 months))

Part C. Q3-1.

Among cfDNA measurments during follow-up, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

- ☐ cfDNA levels
- ☐ cfDNA change between baseline and interim assessment
- ☐ cfDNA change between baseline and end of treatment
- ☐ Other
- ☐ Any of them
- ☐ I think cfDNA during follow-up is not relevant as prognostic marker in MZL

You ticked "Other". So among cfDNA measurments DURING FOLLOW-UP, what is the one you think worthwhile to be evaluated as prognostic for PFS in MZL ?

_____

Part C. Q3-2.

In a prognostic prospect, at what time from treatment start (in months) do you think it would be relevant to measure cfDNA ?

_____
(Please give a number IN MONTHS (e.g. write M2 if you mean 2 months))

Part C. Q4-1.

On which sample would you perform MRD measurement ?

- ☐ Blood
- ☐ Bone marrow
- ☐ I think MRD is not relevant in MZL

Part C. Q4-2.

What technique would you preconize to perform MRD in a MZL trial ?

- ☐ Flow cytometry
- ☐ PCR

Part C. Q4-3

In a prognostic prospect, at what time from treatment start (in months) do you think it would be relevant to measure MRD ?

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(Please give a number IN MONTHS (e.g. write M2 if you mean 2 months))

Part D. Endpoints definitions

As you are still setting up your trial, you're considering to use as clinical endpoints: Progression-free survival, Event-free survival, Time to failure and Time to next treatment.

Part D. Q1.

Considering Progression-free survival, what would you include in the definition of progression?

- ☐ Stable disease after induction (=2 months after treatment start)
- ☐ Progressive disease according to Cheson &al., 2014
- ☐ Relapse of disease
- ☐ Transformation of MZL into a DLBCL
- ☐ Add-on of a new therapy
- ☐ Grade 3-4 adverse events
- ☐ Treatment discontinuation due to adverse events
- ☐ Refusal of patient / Patient's consent withdrawal
- ☐ Lymphoma-related death
- ☐ Death from another origin than lymphoma
- ☐ Death of any cause
- ☐ Last follow-up

Part D. Q2.

Considering Event-free survival, what would you include in the definition of event?

- ☐ Stable disease after induction (=2 months after treatment start)
- ☐ Progressive disease according to Cheson &al., 2014
- ☐ Relapse of disease
- ☐ Transformation of MZL into a DLBCL
- ☐ Add-on of a new therapy
- ☐ Grade 3-4 adverse events
- ☐ Treatment discontinuation due to adverse events
- ☐ Refusal of patient / Patient's consent withdrawal
- ☐ Lymphoma-related death
- ☐ Death from another origin than lymphoma
- ☐ Death of any cause
- ☐ Last follow-up

Part D. Q3.

Considering Time to failure, what would you include in the definition of failure?

- ☐ Stable disease after induction (=2 months after treatment start)
- ☐ Progressive disease according to Cheson &al., 2014
- ☐ Relapse of disease
- ☐ Transformation of MZL into a DLBCL
- ☐ Add-on of a new therapy
- ☐ Grade 3-4 adverse events
- ☐ Treatment discontinuation due to adverse events
- ☐ Refusal of patient / Patient's consent withdrawal
- ☐ Lymphoma-related death
- ☐ Death from another origin than lymphoma
- ☐ Death of any cause
- ☐ Last follow-up

Part D. Q4.

Considering Time to next treatment, what would you include in the definition of next treatment?

- ☐ Stable disease after induction (=2 months after treatment start)
- ☐ Progressive disease according to Cheson &al., 2014
- ☐ Relapse of disease
- ☐ Transformation of MZL into a DLBCL
- ☐ Add-on of a new therapy
- ☐ Grade 3-4 adverse events
- ☐ Treatment discontinuation due to adverse events
- ☐ Refusal of patient / Patient's consent withdrawal
- ☐ Lymphoma-related death
- ☐ Death from another origin than lymphoma
- ☐ Death of any cause
- ☐ Last follow-up