SUPPLEMENTARY METHODS

Multicenter comparison of Molecular Tumor Boards in the Netherlands: definition, composition, methods and targeted therapy recommendations

Bart Koopman, MD, Harry J. M. Groen, MD, PhD, Marjolijn J. L. Ligtenberg, PhD, Katrien Grünberg, MD, PhD, Kim Monkhorst, MD, PhD, Adrianus J. de Langen, MD, PhD, Mirjam C. Boelens, PhD, Marthe S. Paats, MD, PhD, Jan H. von der Thüsen, MD, PhD, Winand N. M. Dinjens, PhD, Nienke Solleveld, PhD, Tom van Wezel, PhD, Hans Gelderblom, MD, PhD, Lizza E. Hendriks, MD, PhD, Ernst Jan M. Speel, PhD, Tom E. Theunissen, PhD, Leonie I. Kroeze, PhD, Niven Mehra, MD, PhD, Berber Piet, MD, PhD, Anthonie J. van der Wekken, MD, PhD, Arja ter Elst, PhD, Wim Timens, MD, PhD, Stefan M. Willems, MD, PhD, Ruud W. J. Meijers, PhD, Wendy W. J. de Leng, PhD, Anne S. R. van Lindert, MD, Teodora Radonic, MD, PhD, Sayed M. S. Hashemi, MD, Daniëlle A. M. Heideman, PhD, Ed Schuuring, PhD, Léon C. van Kempen, PhD

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1. Survey used to systematically perform interviews with MTB participants

General questions

1. What is your name, profession and in what center are you employed?
2. Does the center you are employed in harbor an MTB and if yes, since when?

Scope and value of the MTB

3. What is the value of an MTB as opposed to regular cancer type-specific multidisciplinary team (MDT) meetings?
4. How many cases are discussed in an MTB meeting, on average?
5. What kind of cases are discussed within the MTB?
6. What cancer types can be discussed in the MTB? What is the distribution of cancer types discussed?
7. Do you consider your MTB as a national expert center in one or more of these cancer types?

Logistics and composition of the MTB

8. What is the frequency of MTB meetings? Are you satisfied with this?
9. How much time is reserved for an MTB meeting?
10. What is the turnaround time of the MTB? This is the time from submission of a case for review until return of a recommendation.
11. Does the MTB discuss cases from regional/peripheral hospitals? If yes, which hospitals?
12. If yes, does the MTB offer the possibility to these regional/peripheral hospitals to attend MTB meetings by means of video conferencing?
13. Does the MTB have a chairman and if yes, what is his or her profession?
14. Which health professionals are represented in the MTB?
15. Do these professionals always attend the MTB meetings?
16. Would you prefer a different composition for the MTB meetings?
17. What is the responsibility of the different professionals attending the MTB meetings?
18. Which professionals must be represented as a minimum in an MTB?

**Decision-making methodology of the MTB**

19. How does the MTB reach a decision?
20. What kind of information (i.e. clinical history, molecular testing results) is used to reach a decision?
21. Which molecular testing results can be discussed in the MTB?
22. Which (online) data- and knowledge bases are used to reach a decision (*see form on page 5*)?
23. Concerning the recommendations provided by the MTB:
   a. How often does the MTB recommend (1) targeted therapy; (2) a clinical trial; (3) standard, non-targeted therapy or (4) no treatment?
   b. How often is the recommendation for targeted therapy different from the standard treatment?
   c. How often is ‘off-label’ targeted therapy recommended?
   d. How often is a Named Patient Program recommended?
24. How does the MTB cope with not being able to achieve a recommendation (for example, by calling in expertise from another center or by performing additional tests)?
25. What (clinical) trials are recommended by the MTB?
26. Does the MTB have sufficient insight into the availability of clinical trials?
27. Are you aware of the MTB-app that was designed for this, and do you use it?
28. How does the MTB handle results from the Hartwig Medical Foundation?

Reporting and registration of MTB cases

29. Do you have a local database in which you register cases discussed in the MTB? If yes, what kind of database, and what is registered?

30. How is the MTB recommendation communicated with the treating physician?

31. Is there a report with the MTB recommendation that ends up in the electronic patient record? If not, would you consider such a report of value?

32. Are patients followed up after the MTB recommendation? If not, does the MTB receive feedback on the results of a treatment recommended by the MTB?

View on harmonization and collaboration between MTBs

33. Has the MTB ever been consulted by another MTB? If yes, which, and how often does this occur?

34. Does the MTB ever consult other MTBs? If yes, which, and how often does this occur?

35. Does the MTB feel the need for an overarching expert board, in which complex cases can be forwarded to? If yes, what do you expect to be the functioning of this expert board?

36. Does the MTB want to be part of a national expert network?

37. Does the MTB want to play an active role in the formation of a national expert network?

38. Is there support from the MTB to cooperate with other MTBs in a shared national database for the registration of molecular findings, treatment recommendations and follow-up?

39. What is necessary to achieve the establishment of a knowledge network between MTBs?
2. Form used in assessing data- and knowledge bases used for decision-making

| Data Source | Used in MTB decision-making process |
|-------------|-------------------------------------|
|             | YES | NO |
| 1000 Genomes Browser |     |    |
| Cancer Genome Interpreter |     |    |
| cBioPortal |     |    |
| CIViC |     |    |
| ClinicalTrials.gov |     |    |
| ClinVar |     |    |
| COSMIC |     |    |
| dbSNP |     |    |
| DGIdb |     |    |
| Ensembl |     |    |
| ESMO guidelines |     |    |
| ExAC |     |    |
| InterVar |     |    |
| JAX-CKB |     |    |
| MTB-app |     |    |
| Trialregister.nl |     |    |
| OncoKB |     |    |
| Oncoline |     |    |
| PCT MD Anderson |     |    |
| PubMed |     |    |
| RefSeqGene |     |    |
| VarSome |     |    |
| Local data- or knowledge base |     |    |
| Others (fill in manually): |     |    |
3. Template for submitting a case for the comparative study of MTB recommendations

(English translation of the original version in Dutch)

(starts on next page)
The template below serves to contribute a fictional or anonymized case for use in the 1st national ring trial of MTB cases. Some affairs to take into account:

- The case can be fictional or anonymized. A fictional case should be realistic. An anonymized case must NOT contain traceable information such as date of birth, record numbers or specific calendar months or years in the clinical information.
- It is possible that the organizers will adjust your case to optimize it for use in the ring trial.
- If relevant, you may send in images or other appendices supporting the case attached to the e-mail.

1. NAME OF CONTRIBUTING MTB

| 1.1 NAME MTB | Click here to enter text. | Name of the MTB (for example: “Molecular Tumor Board Groningen”) |

2. MTB INQUIRY

| 2.1 Inquiry | Click here to enter text. | What information is required from the MTB? |

3. CASE INFORMATION

| 3.1 Patient age | Click here to enter text. | NOT date of birth; fill in the absolute age OR an age category (for example, 50-55 years) |
| 3.2 Patient sex | ☐ Male ☐ Female ☐ Unknown | Sex of the patient; if you do not wish to share this, select “unknown” |

4. CLINICAL INFORMATION

| 4.1 Type of cancer | ☐ Lung cancer ☐ Colorectal cancer ☐ Melanoma ☐ GIST | Cancer type category; for the 1st national ring trial of MTB cases, please only use one of the four PATH cancer types |
| 4.2 Histological diagnosis and subclassification | Click here to enter text. | The histological diagnosis (for example: lung adenocarcinoma; mucosal melanoma) |
| 4.3 Stage | TNM: Click here to enter text. Stage: Click here to enter text. | TNM classification and/or cancer staging |
| 4.4 Relevant patient history | Click here to enter text. | For example: previous malignancies, previous therapy for the current malignancy including response, previous molecular findings and current clinical situation, including degree of metastasizing, ECOG performance score (0-4); please only use time intervals and avoid specific calendar months or years |

5. MOLECULAR FINDINGS IN CURRENT SAMPLE (fill in at least one field)
5.1 Mutations

| Gene | cVariant | pVariant | VAF | Test |
|------|----------|----------|-----|------|

Please indicate for each finding: (1) HUGO symbol, (2) nucleotide- and (3) protein change according to HGVS annotation; (4) variant allele frequency and (5) test with which the alterations were found (i.e.: NGS, WGS).

5.2 Copy-number variants (CNV)

| Gene | Afwijing | Test |
|------|---------|------|

Please indicate for each finding: (1) HUGO symbol, (2) alteration (amplification/deletion) and (3) test with which the alterations were found (i.e.: FISH, NGS, MLPA).

5.3 Fusion genes

| Gene | Afwijing | Test |
|------|---------|------|

Please indicate for each finding: (1) HUGO symbol, (2) alteration (i.e.: translocation) and (3) test with which the alterations were found (i.e.: FISH, Archer, NanoString).

5.4 Other relevant findings (including non-molecular findings)

Click here to enter text.

For example, immunohistochemic tests (i.e.: ALK, PD-L1) or other relevant tests.

5.5 Tumor cell percentage

Click here to enter text.

Tumor cell percentage; please also provide scoring method (i.e.: estimation by pathologist, NGS, automated count).

6. REMARKS

Click here to enter text.

Other remarks about this case that you wish to provide to the organizer.

Send the completed form to <censored>. If you send more than one case, please use a separate form for each case, and send each form as a separate file. Thank you kindly for your cooperation.
4. Example of document used for comparison of recommendations (case 1A)

(English translation of the original version in Dutch)

(starts on next page)
National comparative study of MTB recommendations

Round 1 of 5, case A, 26 September 2019 (translated from Dutch to English)

CLINICAL INFORMATION

Sex: Female
Age: 57 years

Diagnosis: Stage IV Lung adenocarcinoma

Clinical history:
- Stage IV Lung adenocarcinoma with $EGFR$ P.(L747_A750delinsP), treated with first-line $EGFR$ inhibitor during one year, with partial response
- After progression, biopsy for resistance analysis: $EGFR$ p.(L747_A750delinsP) and $EGFR$ p.(T790M), treated with osimertinib during two years, with partial response

Current situation:
Progression on osimertinib, new biopsy for resistance analysis.

MOLECULAR FINDINGS IN CURRENT SAMPLE

Tumor cell percentage (estimated by pathologist):
40%

Immunohistochemistry:
PD-L1 negative, ALK negative.

Mutation analysis using next-generation sequencing (PATH panel version 2D):
Mutation in $EGFR$: c.2239_2248delinsC p.(L747_A750delinsP), VAF 32%.
Mutation in $BRAF$: c.1799T>A p.(V600E), VAF 10%.
No mutations detected in the hot spots of the other genes in the panel.

Mutation analysis using liquid biopsy (Avenio):
Mutation in $EGFR$: c.2239_2248delinsC p.(L747_A750delinsP), 0.29% variant allele.
No other mutations detected.

Copy-nummer variant analyse middels fluorescentie in-situ hybridisatie:
No amplification of $MET$ or $ERBB2$.

Fusion gene analysis:
No $ROS1$, $RET$ or $NTRK$ fusion gene.

QUESTION

What are the options for targeted therapy?
# Molecular Tumor Board Recommendation

1. **NAME OF PARTICIPATING MTB**
   
   Click here to enter text.

2. **DO YOU HAVE SUFFICIENT INFORMATION? IF NOT, WHAT INFORMATION IS MISSING?**
   
   Click here to enter text.

3. **WHAT IS YOUR RECOMMENDATION BASED ON THE INFORMATION PROVIDED?**
   
   Click here to enter text.

Send the completed form to <censored>