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MET-FISH Evaluation Algorithm: Proposal of a Simplified Method

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Abstract

MET amplifications (METamp) occur in 5% of NSCLC and represent in most case mechanisms of resistance to ALK and/or EGFR-targeted therapies. METamp detection can be performed using different techniques, although Fluorescence In-Situ Hybridization (FISH) remains the gold-standard, especially in the context of subclonality. To date current evaluation algorithms of MET amplifications are time consuming. Aim of the study was to identify a faster, equally reliable diagnostic algorithm for the detection of METamp, which is currently classified in negativity and low/intermediate/high-level amplification. N=497 NSCLC cases with available MET-FISH data had been selected. The results based on the first evaluated 20 cells had been re-calculated and compared with the definitive results based on 60 cells. For n=464 (93.4%) identical results had been obtained when counting 20 cells instead of 60 cells. Thirty-three cases (5.6%) showed a discrepancy, leading to an incorrect upgrade to a higher diagnostic category (n=25) and to an incorrect downgrade (n=8). We propose a simplified, yet equally reliable MET FISH-algorithm: after accurate screening of the whole tumor slide, twenty tumor cells have to be evaluated and results calculated: If the result is negative, or if all criteria of high-level METamp are fulfilled, the case can be signed out as such. All other cases should be considered as equivocal and additional 40 cells have to be counted. Given that, reliable results can be obtained by counting 20 cells only and an "equivocal" category for cases that need further investigation have been clearly defined.

Keywords: Evaluation Algorithm; Fish; MET-Amplification; Non-Small-Cell-Lung Cancer

Introduction

Lung cancer remains the main cause of cancer related deaths worldwide [1]. New therapies targeting specific genetic alterations fundamentally changed the treatment of patients with advanced stage disease [2]. As consequence, the identification of actionable genetic alterations is part of the routine diagnostic setting [3]. One of the most recent targets are aberrations of the *Mesenchymal epithelial transition factor (MET*) [4, 5]. According to current data [4], *MET* is altered in approximately 5% of non-small cell lung cancers (NSCLC) and is considered as adverse prognostic factor [6-11] and a potential predictive marker for response to anti MET therapeutics [12]. MET pathway activation occurs by several mechanisms that affect cancer cell survival, growth, and invasiveness [4, 12]; among those, *MET* amplifications. Preclinical and clinical evidence suggests that *MET* amplifications may occur as primary oncogenic driver in subsets of treatment-naive lung cancers as well

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as a secondary driver of acquired resistance after treatment with targeted therapies [12]. *MET* copy number gains arise from two distinct processes: polysomy and amplification [13]. While polysomy occurs in cases of chromosomal duplication, true amplification occurs in the setting of focal gene duplication and represents a real oncogenic driver [14, 15]. MET inhibition is now confirmed to lead to clinically meaningful antitumor activity with rapid and durable response and low side effects, especially in the context of MET exon 14 skipping mutations or higher level of amplifications [10, 16, 17].

MET Amplification as Resistance Mechanism in *EGFR*- or *ALK*-altered NSCLC

MET activation has been implicated as an oncogenic driver in *epidermal growth factor receptor (EGFR)*- or *anaplastic lymphoma kinase (ALK)*-positive NSCLC and can mediate primary and secondary resistance to ALK and EGFR tyrosine kinase inhibitors (TKI) [18, 19]. MET inhibition may overcome ALK resistance combining MET and ALK inhibition [19, 20] or analogously, combining MET and anti-EGFR inhibition (erlotinib) [21] to overcome *MET* amplification mediated resistance to EGFR inhibition [22].

Identification of *MET* Amplification

The definition of clinically relevant *MET* amplification however has been a long-debated topic and several criteria have been proposed. *MET* amplification can be identified through different molecular techniques, however, the most widely used method in the clinical setting remains Fluorescence *In-Situ* Hybridization (FISH), also allowing the detection of the exact number of gene copies per cell. Numerous ongoing trials enrolling *MET* amplified NSCLC, show that cut-offs for the definition of *MET* amplification vary [22]. Recently, early data from clinical studies point out [12, 16] that a high-level amplification is necessary to obtain a significant clinical response [16]. As the level of amplification seems to be of prognostic [4, 23] and predictive value [5], FISH remains the most reliable, fast and cost-effective method for the identification of *MET* amplification in the clinical setting [4]. However a unique definition of high-level amplification is still debated. Some authors propose to use the *MET*/centromere 7 (CEP7) copy number ratio [16, 24, 25]. As described by Schildhaus et al [23], *MET* amplification can also co-occur in the context of amplification of the centromere, leading to a ratio < 2, so that the author has proposed a more complex approach including both *MET* gene copy number amplification and *MET*/centromere 7 copy number ratio. This approach has also been preferred in numerous large clinical trials (such as NCT02414139 NCT01610336, NCT01982955 (INSIGH study), and NCT02143466 (TATONN study)) [22]. In addition, in a very recent study [4] Overbeck et al propose a new category of *MET* high-level amplification identifying the higher unequivocal *MET*-amplification level, defined as average *MET* gene copy number of ≥ 10 independently from the *MET*/centromere 7 copy number ratio. With a steadily increasing number of cases, currently applied FISH-criteria can be time-consuming in the daily clinical setting and sometimes may not even be possible in the case of very small biopsies, not reaching the required number of tumor cells. Therefore, the aim of the current work was to develop a faster and equally reliable *MET*-FISH evaluation algorithm that allows the identification of all potentially relevant *MET*-amplification levels in basically all patient samples.

Materials and Methods

Case Collection

The archives of the Institute of Pathology at the University Hospital of Cologne, Cologne, Germany and of the Institute of Pathology at *Klinikum Stuttgart*, Stuttgart, Germany have been searched retrospectively for NSCLC cases at every stages, for which *MET*-FISH analysis has been performed as part of the routine diagnostic work-up according to the internal protocol of the Network Genomic Medicine established in Cologne. For the purpose of this study, only biopsy or resection specimens have been included in the study resulting in n=400 consecutive cases derived from the Institute of Pathology of the University Hospital of Cologne and n=97 consecutive cases from the Institute of Pathology at *Klinikum Stuttgart*. Cytology samples were excluded as specific cut-off criteria were established on formalin-fixed paraffin-embedded (FFPE) tissues samples. Of n=497 cases, n=400 (80.5%) were classified as negative, n=60 (12.1%) as low-level amplification, n=11 (2.2%) as intermediate-level amplification, n=26 (5.2%) as high-level amplification.

Histomorphological Analysis

Histology was reviewed by 3 experienced pathologists (AMS, RC and RB). The diagnosis of NSCLC was confirmed in all cases. Prior to the study, approval by the local ethics committee had been granted and all patients had signed written informed consent.

Fluorescence *In-Situ* Hybridization (FISH)

MET-FISH was performed as part of the routine diagnostic setting using a commercially available FISH probe Zytolight® SPEC *MET*/CN7 Dual color Probe (product nr. Z-2087-200) and its implementation kit (product nr. Z-2028-5/-20) provided by ZytoVision (ZytoVision GmbH, Bremerhaven, Germany) according to manufacturer's instructions. The probe is composed by ZyGreen-marked (excitation 503 nm/ emission 528 nm) gene-sequence including the *MET*-region and by ZyOrange-marked (excitation 547 nm, emission 572 nm) gene-sequence including the centromeric alphasatellite-region D7Z1 of chromosome 7. Slides were reviewed at high magnification power (×63) and scored according to previous

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published guidelines [23]: the entire tumor area was initially screened and the spots with most signals were selected for further analysis. A total number of n=60 cells derived from 3 areas of 20 continuous cells each were counted. As previously described by our group, green *MET* signals and orange CEP7 were counted during routine diagnostic defining 4 groups of amplification status [23]:

1. High-level amplification defined as tumors with MET/CEP7 ratio ≥ 2.0 or an average MET gene copy number per cell of ≥ 6.0 or ≥ 10% of tumor cells containing ≥ 15 MET signals.
2. Intermediate-level of gene copy number (GCN) gain defined as ≥ 50% of cells containing ≥ 5 MET signals and criteria for high-level amplification not being fulfilled.
3. Low-level of gene copy number gain defined as ≥ 40% of tumor cells showing ≥ 4 MET signals and criteria for high-level amplification or intermediate-level of gene copy number gain not being fulfilled.
4. All other tumors were classified as negative.

An example of each category is depicted in Figure 1. In order to verify, whether a more effective evaluation algorithm was possible, the results of the original reports were pulled and re-calculated first using only the first counted 20 cells and then compared to the final result based on 60 counted cells. In both cases the same endpoints (*MET* mean GCN, *CEP7* mean GCN, *MET/CEP7* GCN-ratio and number of cells with ≥ 4/ ≥ 5/ ≥ 15 *MET* signals) were used and the cases were classified according to the following categories:

1. Identical results when counting 20 and when counting 60 cells.
2. Discrepant results leading to a potential upgrade to a higher category when counting only 20 cells.
3. Discrepant results leading to a potential downgrade to a lower category when counting only 20 cells.

Data Analysis

Automated evaluation of the number of signals of *MET*, *CEP7* as well as calculation of *MET/CEP7* ratio and identification of low- /intermediate- / high-level amplification were performed using the FileMaker® software and Microsoft Office Excel.

Results

The reported frequency of *MET* positivity was similar to the main literature data [4, 23]. The dataset of n=497 cases was distributed as follow: (i.) n=26 cases showed high-level amplification. Five of them would have been now classified as Top-level according to the new classification proposed by Overbeck and colleagues; (ii.) n=11 intermediate-level amplification. (iii.) n=60 low-level amplification; (iv.) n=400 negative result. Comparing the results after counting 20 or 60 cells, high concordance was observed. In details, for n=464 (93.4%) cases identical results were obtained when counting only 20 cells instead of 60 cells were obtained. N=25 cases (5.0%) cases would be upgraded to higher category when counting only 20 cells. N=8 cases (1.6%) would be downgraded counting only 20 cells (Figure 2 and Supplementary Table 1). The results obtained from our re-analysis lead to the proposal of the following diagnostic algorithm, which allows a more rapid, but equally reliable and precise evaluation of *MET* gene copy numbers (Figure 3). For all cases classified as negative, the analysis is completed after counting 20 representative cells and the case can be signed out as such. Cases classified as high-level amplification by fulfilling all three criteria (*MET*-GCN ≥ 6, at least 10% of tumor cells containing ≥ 15 MET signals and *MET*/CEP7 ratio ≥ 2) can be signed out as high-level amplification, otherwise (i.e. if only one or two of the criteria for high-level amplification are fulfilled) additional 40 cells have to be evaluated. For all cases that reach the criteria for low-level or intermediate-level amplification, the evaluation of additional 40 cells is mandatory. Given the current evidence of a significant prognostic value of top-level amplifications, defined by gene copy number higher then 10, we suggest including this new category as proposed by Schildhaus and colleagues [5].

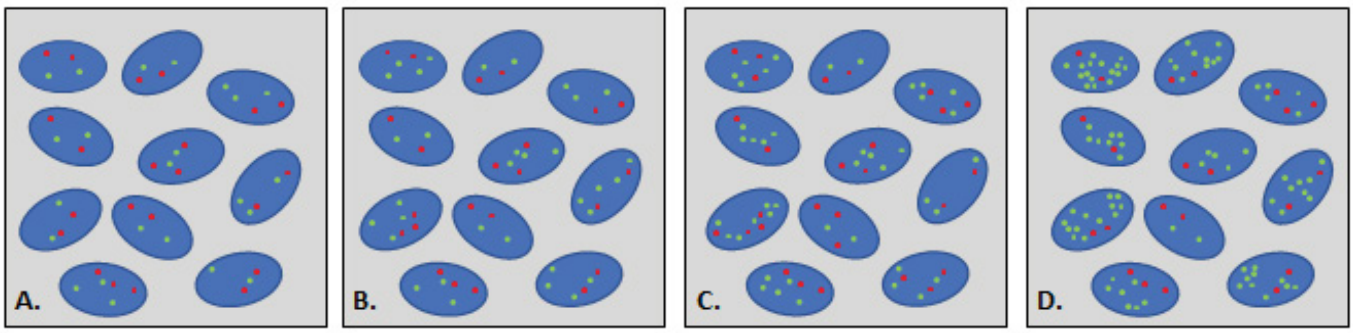

Figure 1: Different level of amplification. Red dot: copy of centromere 7, green dot: copy of *MET* gene. A. Negativity; B. Low-level amplification; C. intermediate-level amplification; D. high-level amplification.

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A. Results after counting 20 cells (n = 497)

B. Stratification of discordant results (n = 33 of 497, p = 6.6 %)

Downgrade of results	n (p)
to intermediate-level *MET*amp	1 (0.2 %)
to low-level *MET*amp	2 (0.4 %)
to negative result	5 (1.0 %)

Upgrade of results	n (p)
to low-level *MET*amp	9 (1.8 %)
to intermediate-level *MET*amp	9 (1.8 %)
to high-level *MET*amp	7 (1.4 %)

Figure 2: Comparison of results after counting 20 or 60 cells. A. Concordant results have obtained in n=464 (93.4%) of cases, discordant results in n=33 (6.6%) cases. B. Analysis of the n=33 discrepant cases after counting 20 or 60 cells. 8 cases (1,6%) would be downgraded in a lower diagnostic category after counting only 20 cells as following: n=5 (1.0%) downgraded to negative result instead of low-level amplification; n=2 (0.4%) downgraded to low-level instead of intermediate-level amplification; n=1 (0.2%) downgraded to intermediate-level instead of high-level amplification. 25 cases (5.0%) would be upgraded to higher category when counting only 20 cells: n=9 (1.8%) upgraded to low-level result instead on negative; n=9 (1.8%) upgraded to intermediate-level instead of low-level amplification; n=5 (0.4%) upgraded to high-level instead of low- or intermediate-level amplification.

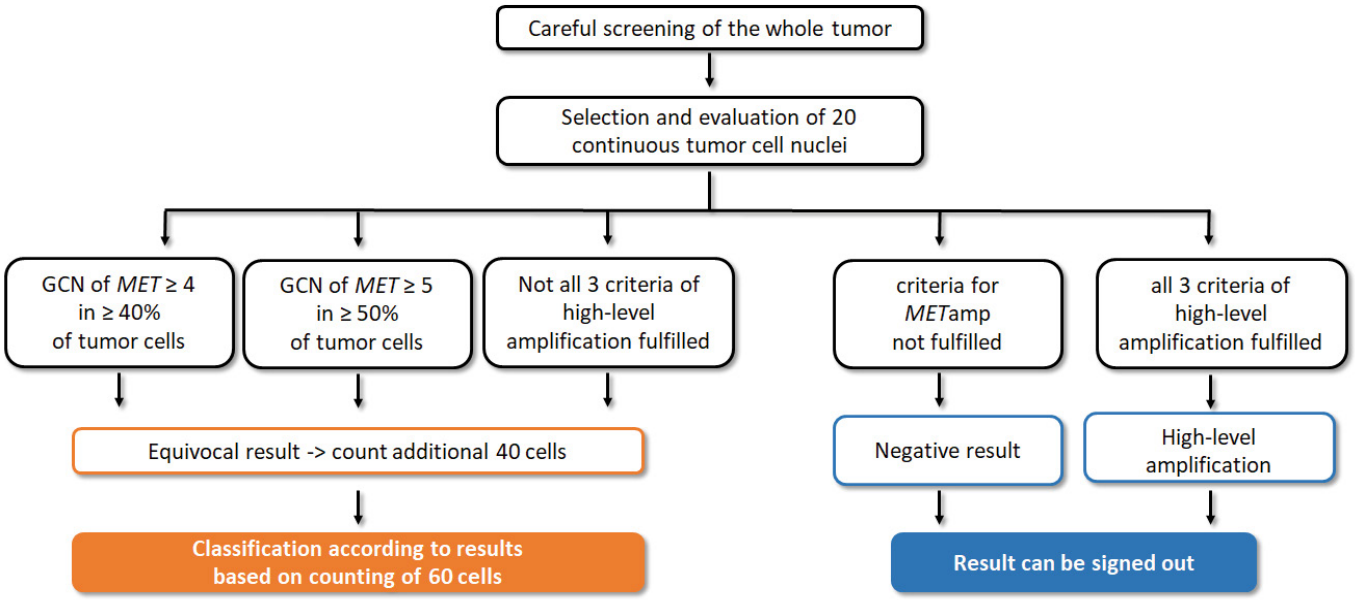

Figure 3: Diagnostic algorithm of MET amplification. After screening the whole tumor slide, the area with greater number of signals per cell is evaluated counting 20 cells. In case of preliminary low-level or intermediate-level amplification, or just one/two criteria for high-level amplification are fulfilled, 40 more cells need to be counted. The final result is based on the evaluation of 60 cells according to previous described criteria. In case of negative result as well as if all three criteria for high-level amplification are fulfilled, the analysis can be signed down.

Discussion and Conclusions

The identification of *MET* genetic alterations represents a crucial point in the molecular assessment of non-small cell lung cancer in advance stage of disease since *MET* may act both as primary driver and as mechanism of resistance to ALK-/EGFR- delivering therapies [12, 18, 19]. Over the last two years, the importance of *MET* alterations has further grown since two drugs targeting *MET*, capmatinib [5] and tepotinib [26], obtained FDA approval. With a steadily increasing number of cases of lung cancer needing a molecular characterization and the fact that FISH currently represents the gold-standard for detection of *MET* amplifications, *MET* FISH analyses can be time-consuming when using currently applied evaluation criteria. Clear cut-off criteria for *MET* amplification remain debated, but the most recent studies on *MET* amplifications agree that higher levels of amplification better respond to *MET* targeted therapies in clinical studies [5, 26] and are associated with poorer prognosis [4]. The

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use of next generation sequencing in the assessment of *MET* amplification, although time-sparing is not suggested since the sensibility in not superior and it provides no description concerning any subclonal variation [6]. The use of immunohistochemistry is as well not recommended for the identification of *MET* amplification, since the specificity is too low, as already published by our group [27]. In this work an updated, shorter, yet equally reliable algorithm for the evaluation of *MET* amplification has been presented, improving the current diagnostic algorithm [23]. According to the results based on n=497 unselected, consecutive *MET* FISH analyses of NSCLC, the same results are obtained in 93.4% (n=464) of cases when counting 20 cells instead of 60 cells. Of thirty-three (6.6%) discordant cases, n=25 (5.0%) would have been upgraded and n=8 (1.6%) would have been downgraded when counting only 20 cells, as listed in the results section and in Figure 2. An upgrade from negative result to low-level amplification (n=9, 1.8%) as well as an upgrade from low-level to intermediate-level amplification (n=9, 1.8%) can be avoided as cases are added to the "equivocal" category and need counting of additional 40 cells as described by the algorithm. Seven (n=7, 1.4%) cases would have been falsely classified as high-level when only counting 20 cells. However, this relevant misclassification can be avoided, if only cases that fulfil all three possible criteria for high-level amplification (MET/CEP7 ratio ≥ 2.0 and average MET gene copy number per cell of ≥ 6.0 and ≥ 10% of tumor cells containing ≥ 15 MET signals) are directly classified as high-level after counting 20 cells. All other cases are classified as "equivocal" and need the counting of additional 40 cells. Of note, this may lead to missing cases with very focal high-level amplification when thorough screening of a case is not performed. If a very focal high-level amplification in therapy-naïve patients however is of clinical relevance needs to be evaluated in further studies. In addition, we believe that the downgrade to a negative result instead of the identification of a clinically not relevant low-level amplification (n=5, 1.0%) can be prevented by thorough slide screening but is rather of no clinical relevance. All cases classifying as low-level (n=2, 0.4%) or intermediate-level (n=1, 0.2%) when using 20 cells will automatically be considered "equivocal" and will be reanalyzed, resulting in counting a total of 60 cells. In contrast to next-generation sequencing based methods, even if in our algorithm just 20 cells are counted, the clonal variations of amplifications are still not missed out, since before starting the count the whole tumor surface has to be screened looking for clonal events. In conclusion, here we propose an updated *MET*-FISH algorithm that provides a much more efficient yet equally reliable way to identify clinically relevant *MET* amplifications in NSCLC in the routine clinical setting, even in the case of very small biopsies.

Conflict of Interest

RB provided lectures and was part of Advisory Boards for AbbVie, Amgen, AstraZeneca, Bayer, BMS, Boehringer-Ingelheim, Illumina, Lilly, Merck-Serono, MSD, Novartis, Qiagen, Pfizer, Roche, Targos MP Inc. RB is Co-Founder and Scientific Advisor for Targos Mol. Pathology Inc. RB is Testifying Advisor for MSD in GBA-Assessment for Pembrolizumab. RB has received funding from the Deutsche Krebshilfe for the Network Genomic Medicine. SMB has received speaker honoraria and personal fees from Pfizer, Novartis, Roche, Bayer, AstraZeneca, Molecular Health, GSK, MSD and Targos; speaker honoraria and non-financial support from BMS; non-financial support from Janssen. The authors declare no further conflict of interest. RC was supported by the Else Kröner-Fresenius Stiftung (2016-Kolleg.19). AMS, CA and BH were supported by Roche Pharma AG. The authors have no further conflict of interest to disclaim.

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SUPPLEMENTARY DATA

Supplementary: Table 1

General data	Evaluation of 20 cells					Evaluation of 60 cells					Comparison of results	
Case nr.	high-level amplification			intermediate-level amplification	low-level amplification	high-level amplification			intermediate-level amplification	low-level amplification	Results after 20 cells	Results after 60 cells
	MET/CEP Ratio ≥ 2	MET GCN ≥ 6	≥ 10 % of cells with MET-GCN ≥ 15	≥ 50 % of cells with MET-GCN ≥ 5	≥ 40 % of cells with MET-GCN ≥ 4	MET/CEP Ratio ≥ 2	MET GCN ≥ 6	≥ 10 % of cells with MET-GCN ≥ 15	≥ 50 % of cells with MET-GCN ≥ 5	≥ 40 % of cells with MET-GCN ≥ 4		
1	no	no	no	no	55 % ≥ 4	no	no	no	no	48 % ≥ 4	low-level	low-level
2	no	no	no	no	no	no	no	no	no	no	negative	negative
3	no	no	no	no	no	no	no	no	no	no	negative	negative
4	no	no	no	no	no	no	no	no	no	no	negative	negative
5	no	no	no	no	no	no	no	no	no	no	negative	negative
6	no	no	no	no	no	no	no	no	no	no	negative	negative
7	no	no	no	no	no	no	no	no	no	no	negative	negative
8	no	no	no	no	no	no	no	no	no	no	negative	negative
9	no	no	no	no	50 % ≥ 4	no	no	no	no	60 % ≥ 4	low-level	low-level
10	no	no	no	no	no	no	no	no	no	no	negative	negative
11	no	no	no	no	no	no	no	no	no	no	negative	negative
12	no	no	no	no	no	no	no	no	no	no	negative	negative
13	no	no	no	no	no	no	no	no	no	no	negative	negative
14	no	no	no	no	no	no	no	no	no	no	negative	negative
15	no	no	no	no	no	no	no	no	no	no	negative	negative
16	no	no	no	no	no	no	no	no	no	no	negative	negative
17	no	no	no	no	no	no	no	no	no	no	negative	negative
18	no	no	no	no	no	no	no	no	no	no	negative	negative
19	5.67	11.90	45 % ≥ 15	no	no	5.08	10.67	28 % ≥ 15	no	no	high-level	high-level
20	no	no	no	no	no	no	no	no	no	no	negative	negative
21	no	no	no	no	no	no	no	no	no	no	negative	negative
22	no	no	no	no	no	no	no	no	no	no	negative	negative
23	no	6.95	no	no	no	no	7.70	no	no	no	high-level	high-level
24	no	no	no	no	no	no	no	no	no	no	negative	negative
25	no	no	no	no	no	no	no	no	no	no	negative	negative
26	no	no	no	no	no	no	no	no	no	no	negative	negative
27	no	no	no	no	no	no	no	no	no	no	negative	negative
28	no	no	no	no	no	no	no	no	no	no	negative	negative
29	no	no	no	no	no	no	no	no	no	no	negative	negative
30	no	no	no	no	no	no	no	no	no	no	negative	negative
31	no	no	no	no	no	no	no	no	no	no	negative	negative
32	no	no	no	50 % ≥ 5	no	no	no	no	no	57 % ≥ 4	intermediate-level	low-level
33	no	no	no	55 % ≥ 5	60 % ≥ 4	no	6.15	no	no	no	intermediate-level	high-level
34	no	no	no	no	no	no	no	no	no	no	negative	negative
35	no	no	no	no	no	no	no	no	no	52 % ≥ 4	negative	low-level
36	no	no	no	no	no	no	no	no	no	no	negative	negative
37	no	no	no	no	40 % ≥ 4	no	no	no	no	53 % ≥ 4	low-level	low-level

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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38	no	no	no	no	no	no	no	no	no	no	negative	negative
39	no	no	no	no	no	no	no	no	no	no	negative	negative
40	no	no	no	no	no	no	no	no	no	no	negative	negative
41	no	no	no	no	no	no	no	no	no	no	negative	negative
42	no	no	no	no	45 % ≥ 4	no	no	no	no	42 % ≥ 4	low-level	low-level
43	no	no	no	no	no	no	no	no	no	no	negative	negative
44	no	no	no	no	no	no	no	no	no	no	negative	negative
45	no	no	no	no	no	no	no	no	no	no	negative	negative
46	2.21	no	no	no	no	no	no	no	no	no	high-level	negative
47	no	no	no	no	no	no	no	no	no	no	negative	negative
48	no	no	no	no	65 % ≥ 4	no	no	no	no	68 % ≥ 4	low-level	low-level
49	no	no	no	55 % ≥ 5	75 % ≥ 4	no	no	no	53 % ≥ 5	75 % ≥ 4	intermediate-level	intermediate-level
50	no	no	no	no	65 % ≥ 4	no	no	no	no	62 % ≥ 4	low-level	low-level
51	4.67	11.21	65 % ≥ 15	80 % ≥ 5	85 % ≥ 4	4.17	10.58	28 % ≥ 15	82 % ≥ 5	83 % ≥ 4	high-level	high-level
52	no	no	no	no	no	no	no	no	no	no	negative	negative
53	no	no	no	no	no	no	no	no	no	no	negative	negative
54	no	no	no	no	no	no	no	no	no	no	negative	negative
55	no	no	no	no	no	no	no	no	no	no	negative	negative
56	no	no	no	no	no	no	no	no	no	no	negative	negative
57	no	no	no	no	no	no	no	no	no	no	negative	negative
58	no	no	no	no	no	no	no	no	no	no	negative	negative
59	2.00	no	no	no	80 % ≥ 4	2.00	6.68	no	55 % ≥ 5	78 % ≥ 4	high-level	high-level
60	no	no	no	no	no	no	no	no	no	no	negative	negative
61	5.64	11.02	no	95 % ≥ 5	95 % ≥ 4	5.08	9.90	no	93,33 % ≥ 5	95 % ≥ 4	high-level	high-level
62	no	no	no	no	no	no	no	no	no	no	negative	negative
63	no	no	no	no	no	no	no	no	no	no	negative	negative
64	no	no	no	no	no	no	no	no	no	no	negative	negative
65	no	no	no	no	no	no	no	no	no	no	negative	negative
66	no	no	no	no	no	no	no	no	no	no	negative	negative
67	no	no	no	no	no	no	no	no	no	no	negative	negative
68	no	6.43	no	55 % ≥ 5	80 % ≥ 4	no	6.10	no	55 % ≥ 5	78 % ≥ 4	high-level	high-level
69	no	no	no	no	no	no	no	no	no	no	negative	negative
70	no	no	no	70 % ≥ 5	70 % ≥ 4	no	no	no	52 % ≥ 5	68 % ≥ 4	intermediate-level	intermediate-level
71	no	no	no	no	no	no	no	no	no	no	negative	negative
72	no	no	no	no	no	no	no	no	no	no	negative	negative
73	no	no	no	no	40 % ≥ 4	no	no	no	no	42 % ≥ 4	low-level	low-level
74	no	no	no	no	no	no	no	no	no	no	negative	negative
75	no	no	no	75 % ≥ 5	80 % ≥ 4	no	no	no	63 % ≥ 5	77 % ≥ 4	intermediate-level	intermediate-level
76	no	no	no	no	55 % ≥ 4	no	no	no	53 % ≥ 5	70 % ≥ 4	low-level	intermediate-level
77	no	no	no	no	no	no	no	no	no	no	negative	negative
78	no	no	no	no	no	no	no	no	no	no	negative	negative
79	no	no	no	no	no	no	no	no	no	no	negative	negative
80	no	no	no	no	no	no	no	no	no	no	negative	negative
81	no	no	no	no	no	no	no	no	no	no	negative	negative
82	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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83	no	no	no	no	no	no	no	no	no	no	negative	negative
84	3.08	6.15	no	50 % ≥ 5	65 % ≥ 4	2.50	no	no	no	60 % ≥ 4	high-level	high-level
85	no	no	no	no	no	no	no	no	no	no	negative	negative
86	no	no	no	55 % ≥ 5	60 % ≥ 4	no	no	no	no	57 % ≥ 4	intermediate-level	low-level
87	no	no	no	no	no	no	no	no	no	no	negative	negative
88	no	no	no	60 % ≥ 5	80 % ≥ 4	no	no	no	no	52 % ≥ 4	intermediate-level	low-level
89	no	no	no	no	no	no	no	no	no	no	negative	negative
90	no	no	no	no	65 % ≥ 4	no	no	no	no	60 % ≥ 4	low-level	low-level
91	no	no	no	no	no	no	no	no	no	no	negative	negative
92	no	no	no	no	no	no	no	no	no	no	negative	negative
93	no	no	no	no	no	no	no	no	no	no	negative	negative
94	no	no	no	no	no	no	no	no	no	no	negative	negative
95	no	no	no	no	45 % ≥ 4	no	no	no	no	52 % ≥ 4	low-level	low-level
96	no	no	no	no	no	no	no	no	no	no	negative	negative
97	no	6.55	no	75 % ≥ 5	85 % ≥ 4	no	no	no	no	63 % ≥ 4	high-level	low-level
98	no	no	no	no	no	no	no	no	no	no	negative	negative
99	no	no	no	no	no	no	no	no	no	no	negative	negative
100	no	no	no	no	no	no	no	no	no	no	negative	negative
101	no	no	no	no	no	no	no	no	no	no	negative	negative
102	no	no	no	no	no	no	no	no	no	no	negative	negative
103	2.14	no	no	no	no	no	no	no	no	no	high-level	negative
104	no	no	no	no	45 % ≥ 4	no	no	no	no	45 % ≥ 4	low-level	low-level
105	no	no	no	no	no	no	no	no	no	no	negative	negative
106	no	no	no	55 % ≥ 5	65 % ≥ 4	no	no	no	62 % ≥ 5	77 % ≥ 4	intermediate-level	intermediate-level
107	no	no	no	no	40 % ≥ 4	no	no	no	no	no	low-level	negative
108	no	no	no	no	no	no	no	no	no	no	negative	negative
109	no	no	no	no	no	no	no	no	no	no	negative	negative
110	no	no	no	no	no	no	no	no	no	no	negative	negative
111	no	no	no	no	no	no	no	no	no	45 % ≥ 4	negative	low-level
112	no	no	no	no	no	no	no	no	no	no	negative	negative
113	no	no	no	no	no	no	no	no	no	no	negative	negative
114	no	no	no	no	no	no	no	no	no	no	negative	negative
115	no	no	no	no	no	no	no	no	no	no	negative	negative
116	no	no	no	no	no	no	no	no	no	no	negative	negative
117	no	no	no	no	no	no	no	no	no	no	negative	negative
118	no	no	no	65 % ≥ 5	70 % ≥ 4	no	no	no	60 % ≥ 5	73 % ≥ 4	intermediate-level	intermediate-level
119	2.21	no	no	50 % ≥ 5	60 % ≥ 4	2.55	no	no	65 % ≥ 5	76 % ≥ 4	high-level	high-level
120	no	no	no	no	no	no	no	no	no	no	negative	negative
121	no	no	no	no	no	no	no	no	no	no	negative	negative
122	no	no	no	no	no	no	no	no	no	no	negative	negative
123	2.14	10.60	no	90 % ≥ 5	95 % ≥ 4	2.03	9.02	no	92 % ≥ 5	95 % ≥ 4	high-level	high-level
124	no	no	no	no	50 % ≥ 4	no	no	no	no	42 % ≥ 4	low-level	low-level
125	no	no	no	no	no	no	no	no	no	no	negative	negative
126	no	no	no	no	no	no	no	no	no	no	negative	negative
127	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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128	no	no	no	no	40 % ≥ 4	no	no	no	no	no	low-level	negative
129	no	no	no	no	no	no	no	no	no	no	negative	negative
130	no	no	no	no	no	no	no	no	no	no	negative	negative
131	no	no	no	no	45 % ≥ 4	no	no	no	no	no	low-level	negative
132	no	no	no	no	no	no	no	no	no	no	negative	negative
133	no	no	no	no	no	no	no	no	no	no	negative	negative
134	2.57	7.70	no	80 % ≥ 5	85 % ≥ 4	2.35	6.82	no	73 % ≥ 5	90 % ≥ 4	high-level	high-level
135	no	no	no	no	no	no	no	no	no	no	negative	negative
136	no	no	no	no	40 % ≥ 4	no	no	no	no	43 % ≥ 4	low-level	low-level
137	no	no	no	no	50 % ≥ 4	no	no	no	no	50 % ≥ 4	low-level	low-level
138	no	no	no	no	no	no	no	no	no	no	negative	negative
139	no	no	no	no	40 % ≥ 4	no	no	no	no	no	low-level	negative
140	no	no	no	no	no	no	no	no	no	no	negative	negative
141	no	no	no	no	no	no	no	no	no	no	negative	negative
142	no	no	no	no	no	no	no	no	no	no	negative	negative
143	no	no	no	no	no	no	no	no	no	no	negative	negative
144	no	no	no	no	no	no	no	no	no	no	negative	negative
145	no	no	no	no	no	no	no	no	no	no	negative	negative
146	no	no	no	no	no	no	no	no	no	no	negative	negative
147	no	no	no	no	no	no	no	no	no	no	negative	negative
148	no	no	no	no	no	no	no	no	no	no	negative	negative
149	no	no	no	no	no	no	no	no	no	no	negative	negative
150	no	no	no	no	no	no	no	no	no	47 % ≥ 4	negative	low-level
151	no	no	no	no	no	no	no	no	no	no	negative	negative
152	no	no	no	no	no	no	no	no	no	no	negative	negative
153	no	no	no	no	65 % ≥ 4	no	no	no	no	57 % ≥ 4	low-level	low-level
154	no	no	no	no	no	no	no	no	no	no	negative	negative
155	no	no	no	no	no	no	no	no	no	no	negative	negative
156	no	no	no	no	no	no	no	no	no	no	negative	negative
157	no	no	no	no	no	no	no	no	no	no	negative	negative
158	no	no	no	no	50 % ≥ 4	no	no	no	no	50 % ≥ 4	low-level	low-level
159	no	no	no	no	no	no	no	no	no	no	negative	negative
160	no	no	no	no	no	no	no	no	no	no	negative	negative
161	no	no	no	no	no	no	no	no	no	no	negative	negative
162	no	no	no	no	no	no	no	no	no	no	negative	negative
163	no	no	no	no	no	no	no	no	no	no	negative	negative
164	no	no	no	no	no	no	no	no	no	no	negative	negative
165	no	no	no	no	no	no	no	no	no	no	negative	negative
166	no	no	no	65 % ≥ 5	85 % ≥ 4	no	no	no	62 % ≥ 5	75 % ≥ 4	intermediate-level	intermediate-level
167	no	no	no	no	no	no	no	no	no	no	negative	negative
168	2.01	no	no	55 % ≥ 5	70 % ≥ 4	2.44	no	no	57 % ≥ 5	72 % ≥ 4	high-level	high-level
169	no	no	no	no	no	no	no	no	no	no	negative	negative
170	no	no	no	no	55 % ≥ 4	no	no	no	no	52 % ≥ 4	low-level	low-level
171	no	no	no	no	no	no	no	no	no	no	negative	negative
172	no	no	no	no	no	no	no	no	no	no	negative	negative
173	no	no	no	no	no	no	no	no	no	no	negative	negative
174	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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175	no	no	no	no	no	no	no	no	no	no	negative	negative
176	no	no	no	no	no	no	no	no	no	no	negative	negative
177	no	no	no	no	no	no	no	no	no	no	negative	negative
178	no	no	no	no	no	no	no	no	no	no	negative	negative
179	no	no	no	no	no	no	no	no	no	no	negative	negative
180	no	no	no	no	45 % ≥ 4	no	no	no	no	45 % ≥ 4	low-level	low-level
181	no	no	no	no	50 % ≥ 4	no	no	no	no	57 % ≥ 4	low-level	low-level
182	no	no	no	no	no	no	no	no	no	no	negative	negative
183	no	no	no	no	no	no	no	no	no	no	negative	negative
184	no	8.34	no	100 % ≥ 5	100 % ≥ 4	no	8.25	no	97 % ≥ 5	98 % ≥ 4	high-level	high-level
185	no	no	no	no	no	no	no	no	no	no	negative	negative
186	no	no	no	no	no	no	no	no	no	no	negative	negative
187	no	no	no	no	no	no	no	no	no	no	negative	negative
188	no	no	no	no	no	no	no	no	no	no	negative	negative
189	no	no	no	no	no	no	no	no	no	no	negative	negative
190	no	no	no	no	no	no	no	no	no	no	negative	negative
191	no	no	no	no	no	no	no	no	no	no	negative	negative
192	no	no	no	no	no	no	no	no	no	no	negative	negative
193	no	no	no	no	no	no	no	no	no	no	negative	negative
194	no	no	no	no	no	no	no	no	no	no	negative	negative
195	no	no	no	50 % ≥ 5	75 % ≥ 4	no	no	no	no	63 % ≥ 4	intermediate-level	low-level
196	no	no	no	no	no	no	no	no	no	no	negative	negative
197	no	no	no	no	no	no	no	no	no	no	negative	negative
198	no	no	no	no	no	no	no	no	no	no	negative	negative
199	no	no	no	no	no	no	no	no	no	no	negative	negative
200	no	no	no	no	no	no	no	no	no	no	negative	negative
201	no	no	no	no	no	no	no	no	no	no	negative	negative
202	no	no	no	no	no	no	no	no	no	no	negative	negative
203	no	no	no	no	no	no	no	no	no	no	negative	negative
204	no	no	no	no	80 % ≥ 4	no	no	no	no	65 % ≥ 4	low-level	low-level
205	no	no	no	no	no	no	no	no	no	no	negative	negative
206	no	no	no	no	no	no	no	no	no	no	negative	negative
207	no	no	no	no	no	no	no	no	no	no	negative	negative
208	no	no	no	no	no	no	no	no	no	no	negative	negative
209	no	no	no	no	no	no	no	no	no	no	negative	negative
210	no	no	no	no	no	no	no	no	no	no	negative	negative
211	no	no	no	no	no	no	no	no	no	no	negative	negative
212	no	no	no	no	no	no	no	no	no	no	negative	negative
213	no	no	no	no	no	no	no	no	no	no	negative	negative
214	no	no	no	no	no	no	no	no	no	no	negative	negative
215	no	no	no	no	no	no	no	no	no	no	negative	negative
216	no	no	no	no	no	no	no	no	no	no	negative	negative
217	no	no	no	no	no	no	no	no	no	no	negative	negative
218	no	no	no	no	no	no	no	no	no	no	negative	negative
219	no	no	no	no	no	no	no	no	no	no	negative	negative
220	no	no	no	no	no	no	no	no	no	no	negative	negative
221	no	no	no	no	50 % ≥ 4	no	no	no	no	45 % ≥ 4	low-level	low-level

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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222	no	no	no	no	no	no	no	no	no	no	negative	negative
223	no	no	no	no	no	no	no	no	no	no	negative	negative
224	no	no	no	no	no	no	no	no	no	no	negative	negative
225	2.56	14.59	no	80 % ≥ 5	85 % ≥ 4	2.48	13.08	no	67 % ≥ 5	68 % ≥ 4	high-level	high-level
226	no	no	no	no	no	no	no	no	no	no	negative	negative
227	no	no	no	no	75 % ≥ 4	no	no	no	no	70 % ≥ 4	low-level	low-level
228	no	no	no	no	50 % ≥ 4	no	no	no	no	no	low-level	negative
229	no	no	no	no	no	no	no	no	no	no	negative	negative
230	no	no	no	no	55 % ≥ 4	no	no	no	no	45 % ≥ 4	low-level	low-level
231	no	no	no	no	no	no	no	no	no	no	negative	negative
232	no	no	no	no	no	no	no	no	no	no	negative	negative
233	no	7.12	no	95 % ≥ 5	95 % ≥ 4	no	6.40	no	93 % ≥ 5	97 % ≥ 4	high-level	high-level
234	no	no	no	no	no	no	no	no	no	no	negative	negative
235	no	no	no	no	no	no	no	no	no	no	negative	negative
236	no	no	no	no	no	no	no	no	no	no	negative	negative
237	no	no	no	no	no	no	no	no	no	no	negative	negative
238	no	no	no	no	no	no	no	no	no	no	negative	negative
239	no	no	no	no	no	no	no	no	no	no	negative	negative
240	no	no	no	no	no	no	no	no	no	no	negative	negative
241	no	no	no	no	no	no	no	no	no	no	negative	negative
242	no	no	no	no	no	no	no	no	no	no	negative	negative
243	no	no	no	no	no	no	no	no	no	no	negative	negative
244	no	no	no	no	no	no	no	no	no	no	negative	negative
245	no	no	no	no	no	no	no	no	no	no	negative	negative
246	no	no	no	no	no	no	no	no	no	no	negative	negative
247	2.33	no	no	no	50 % ≥ 4	no	no	no	no	50 % ≥ 4	high-level	low-level
248	no	no	no	no	60 % ≥ 4	no	no	no	no	48 % ≥ 4	low-level	low-level
249	no	no	no	no	no	no	no	no	no	no	negative	negative
250	no	no	no	no	no	no	no	no	no	no	negative	negative
251	no	no	no	no	no	no	no	no	no	no	negative	negative
252	no	no	no	no	no	no	no	no	no	no	negative	negative
253	no	no	no	no	60 % ≥ 4	no	no	no	no	43 % ≥ 4	low-level	low-level
254	no	no	no	no	no	no	no	no	no	no	negative	negative
255	no	no	no	no	no	no	no	no	no	no	negative	negative
256	no	no	no	no	no	no	no	no	no	no	negative	negative
257	no	no	no	no	45 % ≥ 4	no	no	no	no	no	low-level	negative
258	no	no	no	no	no	no	no	no	no	no	negative	negative
259	no	no	no	no	no	no	no	no	no	no	negative	negative
260	no	no	no	no	no	no	no	no	no	no	negative	negative
261	no	no	no	no	75 % ≥ 4	no	no	no	no	52 % ≥ 4	low-level	low-level
262	no	no	no	no	no	no	no	no	no	no	negative	negative
263	no	no	no	no	no	no	no	no	no	no	negative	negative
264	no	no	no	no	no	no	no	no	no	no	negative	negative
265	no	no	no	no	no	no	no	no	no	no	negative	negative
266	no	no	no	no	no	no	no	no	no	no	negative	negative
267	1.03	no	no	no	no	no	no	no	no	no	negative	negative
268	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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269	no	no	no	no	no	no	no	no	no	48 % ≥ 4	negative	low-level
270	no	no	no	no	70 % ≥ 4	no	no	no	no	57 % ≥ 4	low-level	low-level
271	no	no	no	no	45 % ≥ 4	no	no	no	no	45 % ≥ 4	low-level	low-level
272	no	no	no	no	45 % ≥ 4	no	no	no	no	no	low-level	negative
273	no	no	no	no	no	no	no	no	no	no	negative	negative
274	no	no	no	no	no	no	no	no	no	no	negative	negative
275	2.15	9.94	no	80 % ≥ 5	85 % ≥ 4	2.04	9.52	no	85 % ≥ 5	88 % ≥ 4	high-level	high-level
276	no	no	no	no	no	no	no	no	no	no	negative	negative
277	no	no	no	no	no	no	no	no	no	no	negative	negative
278	no	no	no	no	no	no	no	no	no	no	negative	negative
279	no	no	no	no	no	no	no	no	no	no	negative	negative
280	no	no	no	no	no	no	no	no	no	no	negative	negative
281	no	no	no	no	no	no	no	no	no	no	negative	negative
282	no	no	no	no	no	no	no	no	no	no	negative	negative
283	no	no	no	60 % ≥ 5	75 % ≥ 4	no	no	no	no	70 % ≥ 4	intermediate-level	low-level
284	no	no	no	no	no	no	no	no	no	no	negative	negative
285	no	7.85	no	75 % ≥ 5	80 % ≥ 4	2.04	6.63	no	65 % ≥ 5	80 % ≥ 4	high-level	high-level
286	no	no	no	no	no	no	no	no	no	no	negative	negative
287	no	no	no	no	no	no	no	no	no	no	negative	negative
288	no	no	no	no	no	no	no	no	no	no	negative	negative
289	no	no	no	no	no	no	no	no	no	no	negative	negative
290	no	no	no	no	no	no	no	no	no	no	negative	negative
291	no	no	no	no	no	no	no	no	no	no	negative	negative
292	no	no	no	no	no	no	no	no	no	no	negative	negative
293	no	no	no	50 % ≥ 5	80 % ≥ 4	no	no	no	no	62 % ≥ 4	intermediate-level	low-level
294	no	no	no	no	no	no	no	no	no	no	negative	negative
295	no	no	no	no	no	no	no	no	no	no	negative	negative
296	no	no	no	no	no	no	no	no	no	no	negative	negative
297	no	no	no	no	no	no	no	no	no	no	negative	negative
298	no	no	no	no	no	no	no	no	no	no	negative	negative
299	no	no	no	no	no	no	no	no	no	no	negative	negative
300	no	no	no	no	no	no	no	no	no	no	negative	negative
301	no	no	no	no	no	no	no	no	no	no	negative	negative
302	no	no	no	no	no	no	no	no	no	no	negative	negative
303	no	no	no	no	no	no	no	no	no	no	negative	negative
304	no	no	no	no	no	no	no	no	no	no	negative	negative
305	no	no	no	no	no	no	no	no	no	no	negative	negative
306	no	no	no	no	no	no	no	no	no	no	negative	negative
307	no	no	no	no	no	no	no	no	no	no	negative	negative
308	no	no	no	no	no	no	no	no	no	no	negative	negative
309	no	no	no	no	no	no	no	no	no	no	negative	negative
310	no	no	no	no	no	no	no	no	no	no	negative	negative
311	no	no	no	no	no	no	no	no	no	no	negative	negative
312	no	no	no	no	no	no	no	no	no	no	negative	negative
313	no	no	no	no	no	no	no	no	no	no	negative	negative
314	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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315	no	no	no	no	40 % ≥ 4	no	no	no	no	no	low-level	negative
316	no	no	no	no	no	no	no	no	no	no	negative	negative
317	no	no	no	no	no	no	no	no	no	no	negative	negative
318	no	no	no	no	no	no	no	no	no	no	negative	negative
319	no	no	no	no	no	no	no	no	no	no	negative	negative
320	no	no	no	no	no	no	no	no	no	no	negative	negative
321	no	no	no	no	no	no	no	no	no	no	negative	negative
322	no	no	no	no	40 % ≥ 4	no	no	no	no	no	low-level	negative
323	no	no	no	no	no	no	no	no	no	no	negative	negative
324	no	no	no	no	no	no	no	no	no	no	negative	negative
325	no	no	no	no	no	no	no	no	no	no	negative	negative
326	no	no	no	no	no	no	no	no	no	no	negative	negative
327	no	no	no	no	no	no	no	no	no	no	negative	negative
328	no	no	no	no	no	no	no	no	no	no	negative	negative
329	no	no	no	no	no	no	no	no	no	no	negative	negative
330	no	no	no	no	no	no	no	no	no	no	negative	negative
331	no	no	no	no	no	no	no	no	no	no	negative	negative
332	no	no	no	no	no	no	no	no	no	no	negative	negative
333	no	no	no	no	no	no	no	no	no	no	negative	negative
334	no	no	no	no	no	no	no	no	no	no	negative	negative
335	no	no	no	no	no	no	no	no	no	no	negative	negative
336	no	no	no	no	no	no	no	no	no	no	negative	negative
337	4.51	7.45	no	85 % ≥ 5	90 % ≥ 4	4.23	7.33	no	87 % ≥ 5	92 % ≥ 4	high-level	high-level
338	no	no	no	no	no	no	no	no	no	no	negative	negative
339	no	no	no	no	no	no	no	no	no	no	negative	negative
340	no	no	no	no	no	no	no	no	no	no	negative	negative
341	no	no	no	no	no	no	no	no	no	no	negative	negative
342	no	no	no	no	no	no	no	no	no	no	negative	negative
343	no	no	no	no	no	no	no	no	no	no	negative	negative
344	no	no	no	no	no	no	no	no	no	no	negative	negative
345	no	no	no	no	no	no	no	no	no	no	negative	negative
346	no	no	no	no	no	no	no	no	no	no	negative	negative
347	no	no	no	no	no	no	no	no	no	no	negative	negative
348	no	no	no	no	50 % ≥ 4	no	no	no	no	62 % ≥ 4	low-level	low-level
349	no	no	no	no	55 % ≥ 4	no	no	no	52 % ≥ 5	63 % ≥ 4	low-level	intermediate-level
350	no	no	no	no	no	no	no	no	no	no	negative	negative
351	no	no	no	no	no	no	no	no	no	no	negative	negative
352	no	no	no	no	no	no	no	no	no	no	negative	negative
353	no	no	no	no	no	no	no	no	no	no	negative	negative
354	2.75	10.05	no	80 % ≥ 5	80 % ≥ 4	3.01	9.93	no	80 % ≥ 5	87 % ≥ 4	high-level	high-level
355	no	no	no	55 % ≥ 5	80 % ≥ 4	no	no	no	no	67 % ≥ 4	intermediate-level	low-level
356	no	no	no	no	no	no	no	no	no	no	negative	negative
357	no	no	no	no	no	no	no	no	no	no	negative	negative
358	no	no	no	no	no	no	no	no	no	no	negative	negative
359	no	no	no	no	no	no	no	no	no	no	negative	negative
360	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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361	no	no	no	no	no	no	no	no	no	no	negative	negative
362	no	no	no	no	no	no	no	no	no	no	negative	negative
363	no	no	no	no	no	no	no	no	no	no	negative	negative
364	no	no	no	no	no	no	no	no	no	no	negative	negative
365	no	no	no	no	no	no	no	no	no	no	negative	negative
366	no	no	no	no	no	no	no	no	no	no	negative	negative
367	no	no	no	no	no	no	no	no	no	no	negative	negative
368	no	no	no	no	65 % ≥ 4	no	no	no	no	58 % ≥ 4	low-level	low-level
369	no	no	no	no	55 % ≥ 4	no	no	no	no	55 % ≥ 4	low-level	low-level
370	no	8.00	no	60 % ≥ 5	60 % ≥ 4	2.33	10.28	no	75 % ≥ 5	78 % ≥ 4	high-level	high-level
371	no	no	no	no	55 % ≥ 4	no	no	no	no	58 % ≥ 4	low-level	low-level
372	no	no	no	no	no	no	no	no	no	no	negative	negative
373	no	no	no	50 % ≥ 5	65 % ≥ 4	no	no	no	no	52 % ≥ 4	intermediate-level	low-level
374	no	no	no	no	no	no	no	no	no	no	negative	negative
375	no	no	no	no	no	no	no	no	no	no	negative	negative
376	no	no	no	no	no	no	no	no	no	no	negative	negative
377	no	no	no	no	no	no	no	no	no	no	negative	negative
378	no	no	10 % ≥ 15	50 % ≥ 5	80 % ≥ 4	no	no	no	no	65 % ≥ 4	high-level	low-level
379	no	no	no	no	no	no	no	no	no	no	negative	negative
380	no	6.39	10 % ≥ 15	no	60 % ≥ 4	no	no	no	53 % ≥ 5	72 % ≥ 4	high-level	intermediate-level
381	2.44	11.25	10 % ≥ 15	90 % ≥ 5	100 % ≥ 4	no	8.55	10 % ≥ 15	77 % ≥ 5	87 % ≥ 4	high-level	high-level
382	no	no	no	no	no	no	no	no	no	no	negative	negative
383	no	no	no	no	no	no	no	no	no	no	negative	negative
384	no	no	no	no	no	no	no	no	no	no	negative	negative
385	no	no	no	no	no	no	no	no	no	no	negative	negative
386	no	no	no	no	no	no	no	no	no	no	negative	negative
387	no	no	no	no	no	no	no	no	no	48 % ≥ 4	negative	low-level
388	no	no	no	no	no	no	no	no	no	no	negative	negative
389	no	no	no	no	no	no	no	no	no	no	negative	negative
390	no	no	no	no	no	no	no	no	no	no	negative	negative
391	no	no	no	no	no	no	no	no	no	no	negative	negative
392	no	no	no	no	50 % ≥ 4	no	no	no	no	60 % ≥ 4	low-level	low-level
393	no	no	no	no	no	no	no	no	no	no	negative	negative
394	no	no	no	no	70 % ≥ 4	no	no	no	no	70 % ≥ 4	low-level	low-level
395	no	no	no	no	no	no	no	no	no	no	negative	negative
396	no	6.45	no	80 % ≥ 5	95 % ≥ 4	no	no	no	65 % ≥ 5	80 % ≥ 4	high-level	intermediate-level
397	no	no	no	no	no	no	no	no	no	no	negative	negative
398	no	no	no	no	no	no	no	no	no	no	negative	negative
399	no	no	no	no	no	no	no	no	no	no	negative	negative
400	no	no	no	no	no	no	no	no	no	no	negative	negative
401	no	no	no	no	no	no	no	no	no	no	negative	negative
402	no	6.12	10 % ≥ 15	75 % ≥ 5	90 % ≥ 4	no	6.10	no	80 % ≥ 5	93 % ≥ 4	high-level	high-level
403	no	no	no	no	no	no	no	no	no	no	negative	negative
404	no	no	no	no	no	no	no	no	no	no	negative	negative
405	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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406	no	no	no	no	55 % ≥ 4	no	no	no	no	40 % ≥ 4	low-level	low-level
407	no	no	no	no	no	no	no	no	no	no	negative	negative
408	no	no	no	no	no	no	no	no	no	no	negative	negative
409	no	no	no	no	no	no	no	no	no	no	negative	negative
410	no	no	no	no	no	no	no	no	no	47 % ≥ 4	negative	low-level
411	no	no	no	no	55 % ≥ 4	no	no	no	no	53 ≥ 4	low-level	low-level
412	no	no	no	no	no	no	no	no	no	no	negative	negative
413	no	6.00	no	65 % ≥ 5	90 % ≥ 4	no	6.50	22 % ≥ 15	72 % ≥ 5	85 % ≥ 4	high-level	high-level
414	no	no	no	no	no	no	no	no	no	no	negative	negative
415	no	no	no	no	no	no	no	no	no	no	negative	negative
416	no	no	no	no	no	no	no	no	no	no	negative	negative
417	no	6.32	no	80 % ≥ 5	100 % ≥ 4	no	6.03	no	78 % ≥ 5	90 % ≥ 4	high-level	high-level
418	no	no	no	no	no	no	no	no	no	no	negative	negative
419	no	no	no	no	no	no	no	no	no	no	negative	negative
420	no	no	no	no	no	no	no	no	no	no	negative	negative
421	no	no	no	no	no	no	no	no	no	no	negative	negative
422	no	no	no	no	no	no	no	no	no	no	negative	negative
423	no	no	no	no	no	no	no	no	no	no	negative	negative
424	no	no	no	no	45 % ≥ 4	no	no	no	no	47 % ≥ 4	low-level	low-level
425	no	no	no	no	no	no	no	no	no	no	negative	negative
426	no	no	no	no	no	no	no	no	no	no	negative	negative
427	no	no	no	no	no	no	no	no	no	no	negative	negative
428	no	no	no	no	no	no	no	no	no	no	negative	negative
429	no	no	no	no	no	no	no	no	no	no	negative	negative
430	no	no	no	75 % ≥ 5	85 % ≥ 4	no	no	no	65 % ≥ 5	85 % ≥ 4	intermediate-level	intermediate-level
431	no	no	no	no	no	no	no	no	no	no	negative	negative
432	no	no	no	no	no	no	no	no	no	no	negative	negative
433	no	no	no	no	no	no	no	no	no	no	negative	negative
434	no	no	no	no	no	no	no	no	no	no	negative	negative
435	no	no	no	no	no	no	no	no	no	no	negative	negative
436	no	no	no	no	no	no	no	no	no	no	negative	negative
437	no	no	no	no	no	no	no	no	no	no	negative	negative
438	no	no	no	no	no	no	no	no	no	no	negative	negative
439	no	no	no	no	no	no	no	no	no	no	negative	negative
440	no	no	no	no	no	no	no	no	no	no	negative	negative
441	no	no	no	no	no	no	no	no	no	no	negative	negative
442	no	no	no	no	no	no	no	no	no	no	negative	negative
443	no	no	no	no	no	no	no	no	no	no	negative	negative
444	no	no	no	no	no	no	no	no	no	no	negative	negative
445	no	no	no	no	no	no	no	no	no	no	negative	negative
446	no	no	no	no	no	no	no	no	no	no	negative	negative
447	no	no	no	no	no	no	no	no	no	no	negative	negative
448	no	no	no	no	no	no	no	no	no	no	negative	negative
449	no	no	no	no	no	no	no	no	no	no	negative	negative
450	no	no	no	no	50 % ≥ 4	no	no	no	no	62 % ≥ 4	low-level	low-level
451	no	no	no	no	no	no	no	no	no	no	negative	negative

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.

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452	no	no	no	no	no	no	no	no	no	no	negative	negative
453	no	no	no	no	no	no	no	no	no	no	negative	negative
454	no	no	no	no	no	no	no	no	no	no	negative	negative
455	no	no	no	no	45 % ≥ 4	no	no	no	no	50 % ≥ 4	low-level	low-level
456	no	no	no	no	no	no	no	no	no	no	negative	negative
457	no	no	no	no	no	no	no	no	no	no	negative	negative
458	no	no	no	no	no	no	no	no	no	no	negative	negative
459	no	no	no	no	no	no	no	no	no	no	negative	negative
460	no	no	no	no	no	no	no	no	no	no	negative	negative
461	no	no	no	no	no	no	no	no	no	no	negative	negative
462	no	no	no	no	no	no	no	no	no	no	negative	negative
463	no	no	no	no	no	no	no	no	no	no	negative	negative
464	no	no	no	no	no	no	no	no	no	no	negative	negative
465	2.34	6.40	20 % ≥ 10	75 % ≥ 5	80 % ≥ 4	2.66	6.54	15 % ≥ 10	74 % ≥ 5	85 % ≥ 4	high-level	high-level
466	no	no	no	no	no	no	no	no	no	no	negative	negative
467	no	no	no	no	no	no	no	no	no	no	negative	negative
468	no	no	no	no	45 % ≥ 4	no	no	no	no	51 % ≥ 4	low-level	low-level
469	no	no	no	no	no	no	no	no	no	no	negative	negative
470	no	no	no	no	no	no	no	no	no	no	negative	negative
471	no	no	no	no	no	no	no	no	no	no	negative	negative
472	no	no	no	no	no	no	no	no	no	no	negative	negative
473	no	no	no	no	no	no	no	no	no	no	negative	negative
474	no	no	no	no	no	no	no	no	no	no	negative	negative
475	no	no	no	no	no	no	no	no	no	no	negative	negative
476	no	no	no	no	40 % ≥ 4	no	no	no	no	43 % ≥ 4	low-level	low-level
477	no	no	no	50 % ≥ 5	60 % ≥ 4	no	no	no	no	53 % ≥ 4	intermediate-level	low-level
478	no	no	no	no	no	no	no	no	no	no	negative	negative
479	no	no	no	no	no	no	no	no	no	no	negative	negative
480	no	no	no	no	no	no	no	no	no	no	negative	negative
481	no	no	no	no	no	no	no	no	no	no	negative	negative
482	no	no	no	no	no	no	no	no	no	no	negative	negative
483	no	8.60	35 % ≥ 10	90 % ≥ 5	95 % ≥ 4	no	8.02	23 % ≥ 10	93 % ≥ 5	97 % ≥ 4	high-level	high-level
484	no	no	no	no	no	no	no	no	no	no	negative	negative
485	no	no	no	no	no	no	no	no	no	no	negative	negative
486	no	no	no	no	no	no	no	no	no	no	negative	negative
487	no	no	no	no	no	no	no	no	no	no	negative	negative
488	no	no	no	no	no	no	no	no	no	no	negative	negative
489	no	no	no	no	45 % ≥ 4	no	no	no	no	55 % ≥ 4	low-level	low-level
490	no	no	no	no	no	no	no	no	no	no	negative	negative
491	no	no	no	no	no	no	no	no	no	no	negative	negative
492	no	no	no	no	no	no	no	no	no	no	negative	negative
493	no	no	no	no	no	no	no	no	no	no	negative	negative
494	no	no	no	no	no	no	no	no	no	no	negative	negative
495	no	no	no	no	no	no	no	no	no	no	negative	negative
496	no	no	no	no	no	no	no	no	no	no	negative	negative
497	no	no	no	no	80 % ≥ 4	no	no	no	no	72 % ≥ 4	low-level	low-level

Citation: Roberta Castiglione, Christina Alidousty, Barbara Holz, Nicolai Duerbaum, Maike Wittersheim, Elke Binot, Sabine Merkelbach-Bruse, Nicolaus Friedrichs, Matthias S Dettmer, Alexander Bosse, Reinhard Buettner and Anne Maria Schultheis. MET-FISH Evaluation Algorithm: Proposal of a Simplified Method. Journal of Cancer Science and Clinical Therapeutics 6 (2022): 411-427.