

Gender: Male | Birth year: 1950 | WHO: 1

Tumor: Skin - Melanoma | Lesions: Brain, CNS, Liver, Lung, Test Lesion, Lymph nodes (abdominal, cervical and supraclavicular) | Stage: IV

Summary

Clinical summary

|                                     |   |  |
|-------------------------------------|---|--|
| Relevant systemic treatment history | 2019  | Therapy1   |
|                                     | ?-6/2020  | Therapy2   |
|                                     | 8/2020-3/2021   | Therapy3   |
|                                     | 2022  | Clinical trial: Trial1   |
|                                     | 2022  | Clinical trial: Trial1 (3 cycles, stop reason: toxicity)                   |
|                                     | 2022  | Clinical trial (tr2): Trial2 (3 cycles, stop reason: toxicity)             |
|                                     | 2022  | Clinical trial: Trial4 (adjuvant, 1 cycle, stop reason: toxicity)          |
|                                     | 2022  | Clinical trial: Trial5 (adjuvant and consolidation, stop reason: toxicity) |
|                                     | 2023  | Therapy4   |
|                                     | Date unknown  | Therapy  |
| Relevant other oncological history  | 2022  | Clinical trial (details unknown)   |
| Previous primary tumor              | Lung adenocarcinoma (diagnosed 6/2021, considered non-active) |  |
| Relevant non-oncological history    | Pancreatitis  |  |
|                                     | Coronary artery bypass graft (CABG)                           |  |

Recent molecular results

Hartwig WGS of ACTN01029999 (13-Jun-2024)

|   |                                  |
|---|----------------------------------|
| Biopsy location                                       | Liver (purity 98%)               |
| Molecular tissue of origin prediction                 | Melanoma (100%)                  |
| Tumor mutational load / burden                        | TML high (185) / TMB high (13.7) |
| Microsatellite (in)stability                          | Stable                           |
| HR status   | Proficient (0.45)                |
| Genes with high driver mutation                       | BRAF                             |
| Amplified genes                                       | MYC                              |
| Deleted genes   | PTEN                             |
| Homozygously disrupted genes                          | PTEN                             |
| Gene fusions  | EML4 - ALK fusion                |
| Virus detection                                       | HPV positive (3 int. detected)   |
| Potentially actionable events with medium/low driver: | PTEN disruption                  |

Approved treatments considered eligible

|                    |
|--------------------|
| Treatment          |
| Not yet determined |

EMC trials that are open and considered eligible and currently have slots available (1 cohort from 1 trial)

| Trial                               | Cohort   | Molecular | Warnings                    |
|-------------------------------------|----------|-----------|-----------------------------|
| Test Trial 1<br>TEST-1<br>(Phase 1) | Cohort B | None      | Undetermined SOC exhaustion |

EMC trials that are open and considered eligible but currently have no slots available (2 cohorts from 2 trials)

| Trial                               | Cohort   | Molecular | Warnings                    |
|-------------------------------------|----------|-----------|-----------------------------|
| Test Trial 1<br>TEST-1<br>(Phase 1) | Cohort A | MSI       | Undetermined SOC exhaustion |
| Test Trial 2<br>TEST-2              | Cohort A | MSI       | None                        |

trial kb trials potentially eligible based on molecular results which are potentially recruiting in The Netherlands (2)

| Event  | Trial title   | NCT number                  |
|--|---|-----------------------------|
| TMB High,<br>TML High,<br>PTEN hom disruption,<br>PTEN disruption,<br>EML4 - ALK fusion,<br>HPV positive | treatment   | <a href="#">NCT00000001</a> |
| MYC amp  | A Phase 1 Study of XYXYXY, a T-Cell-Redirecting Agent Targeting Z, for Advanced Prostate Cancer | <a href="#">NCT00000003</a> |

trial kb trials potentially eligible based on molecular results which are potentially recruiting outside the Netherlands (1)

| Event    | Trial title  | NCT number                  | Country          |
|----------|--|-----------------------------|------------------|
| PTEN del | A Phase 1/2 Randomized Study to Evaluate the Safety and Efficacy of treatment X Plus ... Y, as First-Line Treatment for Participants With Advanced Solid Tumor (acronym) | <a href="#">NCT00000020</a> | Belgium, Germany |

Currently only Belgian and German trials are supported

Molecular Details

Hartwig WGS (ACTN01029999T, 13-Jun-2024)

General

| Purity | TML Status | TMB Status  | MS Stability | HR Status         | DPYD                     | UGT1A1   |
|--------|------------|-------------|--------------|-------------------|--------------------------|--|
| 98%    | High (185) | High (13.7) | Stable       | Proficient (0.45) | *1_HOM (Normal function) | *1_HET (Normal function), *28_HET (Reduced function) |

Predicted tumor origin

| 1. Melanoma   |      |
|---|------|
| Combined prediction score                             | 100% |
| This score is calculated by combining information on: |      |
| (1) SNV types   | 98%  |
| (2) SNV genomic localisation distribution             | 99%  |
| (3) Driver genes and passenger characteristics        | 97%  |

Other cohorts have a combined prediction of 0% or lower

Drivers

| Type                    | Driver                                       | Driver likelihood | Trials in EMC | Trials in trial kb | Best evidence in kb | Resistance in kb |
|-------------------------|--|-------------------|---------------|--------------------|---------------------|------------------|
| Mutation (Hotspot)      | BRAF V600E (4/6 copies)                      | High              |               |                    | Approved            |                  |
| Amplification           | MYC amp, 38 copies                           | High              |               | NCT00000003        |                     |                  |
| Loss                    | PTEN del, 0 copies                           | High              |               | NCT00000020        |                     |                  |
| Known fusion            | EML4 - ALK fusion, exon 6 - exon 20          | High              |               | NCT00000001        | Approved            | Known resistance |
| Disruption (homozygous) | PTEN   | High              |               | NCT00000001        | Approved            | Known resistance |
| Virus                   | HPV positive, 3 integrations detected        | High              |               | NCT00000001        | Approved            | Known resistance |
| Disruption              | PTEN, DEL (1.1 discr. / 1.8 undiscr. copies) | Low               |               | NCT00000001        | Approved            | Known resistance |

Clinical Details

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|                                     |   |  |
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Patient current details (08-Jun-2024)

|                                  |                     |
|----------------------------------|---------------------|
| Unresolved toxicities grade => 2 | Fatigue (2)         |
| Cancer-related complications     | Ascites             |
| Known allergies                  | Wasps (Environment) |
| Recent surgeries                 | 19-May-2024         |

Tumor details (08-Jun-2024)

|                     |                                    |
|---------------------|------------------------------------|
| Measurable disease  | Yes                                |
| CNS lesion status   | Present CNS lesions (active)       |
| Brain lesion status | Present brain lesions (not active) |

Active medication details

| Medication | Administration route | Start date | Stop date | Dosage | Frequency |
|------------|----------------------|------------|-----------|--------|-----------|
| None       |                      |            |           |        |           |

Blood transfusions

| Product                 | Date        |
|-------------------------|-------------|
| Thrombocyte concentrate | 03-Jun-2024 |

Trial Matching Summary

EMC trials and cohorts that meet molecular requirements and may be eligible, but are closed (0)

None

EMC trials and cohorts that are open but considered ineligible (1)

| Trial                  | Cohort   | Molecular | Ineligibility reasons   |
|------------------------|----------|-----------|-------------------------|
| Test Trial 2<br>TEST-2 | Cohort B | None      | Pembrolizumab treatment |