In-/Exclusion criteria

INFORM Registry

INFORM – INdividualized Therapy FOr Relapsed Malignancies in Childhood

Coordinating Investigator Registry: Prof. Dr. med. Olaf Witt

KiTZ Clinical Trial Unit

Kristian Pajtler / Cecilia Zuliani

Tel. +49 6221-56-6913

Email: inform_info@dkfz-heidelberg.de

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In-/Exclusion Criteria

General Inclusion Criteria:

- Children, adolescents and young adults 0 to 40 years old with refractory/relapsed/progressive oncological disease following first, second or third line treatment protocols, including targeted treatment approaches considering entity-specific high risk criteria. High grade gliomas (incl. DIPG), specific soft tissue sarcomas, ETMR and rare tumor diseases included in the STEP Registry, e.g. carcinoma, melanoma, rare gonadal tumors or in the MET Registry, e.g. ACC, ACx, PCC/PGL by SDHB or metastases, MTC, NETs except appendix may be enrolled upon primary diagnosis.

  Contact respective study group chair (or respective national coordinator) in case of further questions on inclusion characteristics of patients.

- Patients can be included up until the age of 40 years, but they must have had their primary diagnosis below the age of 21 years.
- No established curative treatment options
- Life expectancy > 3 months and sufficient general condition (Lansky ≥ 50 or Karnofsky ≥ 50)

  Please estimate life expectancy and general condition critically; patients in a pre-final stage are not eligible for enrolment in INFORM.

- Patient treated in Germany or in one of the partner countries.

  Patients can only be registered if they are treated in Germany or in one of the participating countries.

- First-line treatment within one of the therapy optimization/registry trials of the GPOH or an equivalent protocol, except for primary diagnosis high-grade gliomas (incl. DIPG), specific primary soft tissue sarcomas, ETMR, rare tumor diseases included in the STEP Registry or malignant endocrine tumors included in the MET Registry.
- Inclusion in INFORM Registry discussed with and agreed by respective GPOH entity study group (or with the respective National Coordinator).
- Histopathological/molecular confirmation of clinically suspected diagnosis (Result/confirmation does not have to be available at the time of registration).
- Routine surgery/puncture of the current oncological disease as part of standard of care treatment.

- Time between surgery/puncture of the current oncological disease and receipt of all required samples and information in the INFORM Incoming / Sample Processing Laboratory at the CCU Neuropathology in Heidelberg ≤ 8 weeks.

  After biopsy/puncture, the material should be shipped to the INFORM Incoming / Sample Processing Laboratory at the CCU Neuropathology in Heidelberg A.S.A.P; delay of material arrival in Heidelberg of more than 8 weeks will not be accepted for analysis. If there are any delays due to problems with cost coverage, please contact INFORM for advice.

- For German patients with solid tumors and brain tumors suitable fresh frozen tumor tissue of the current disease episode and Non-malignant germline material will be sent to INFORM Registry for molecular analysis.

  For all patients, these 2 types of tissue are required. Please read the Registration and Shipment Manual carefully, as incomplete submissions will significantly delay the process!

- For all international patients (and German patients with non-solid tumors) already extracted Tumor DNA and Tumor RNA from Fresh Frozen malignant material of the current disease episode as well as DNA from Non-malignant germline material will be sent to INFORM Registry for molecular analysis.

  For all patients, these 2 types of tissue are required. Please read the Registration and Shipment Manual carefully, as incomplete submissions will significantly delay the process!

- Tumor cell content / tumor infiltration / blast content in the submitted tumor material has to be at least 40% (in case of non-solid tumors at least 30% (e.g. ALL-HR, ALL post-SCT, ALL post-CAR-T cell therapy, AML, non-solid Lymphoma and neuroblast-infiltrated bone marrow) as the proportion of tumor cells in these samples can be more reliably assessed than in solid malignancies).

- Written informed consent of the patients and/or the legal guardians.

  Please use the current version 6.0 (from 2023).

- Re-analysis of tumor sample in INFORM from a new biopsy is allowed: at least 6 months after previous INFORM analysis (date of sample receipt incoming lab) or at progression following a clear response (> 25% tumor reduction) to a targeted or immune therapy (after consultation with the INFORM Trial Office).

General Exclusion Criteria:

- The patient does not have confirmation of cost coverage for the INFORM analyses
- Entity specific exclusion criteria: see below 5.3

Entity Specific In-/Exclusion Criteria:

ALL-HR and ALL post-CAR-T cell therapy

Inclusion Criteria:

General:

- Bone marrow involvement and/or extramedullary relapse of ALL (> 30% leukemic blasts)

Specific ALL-HR:

- 1st and higher T-ALL relapse
- 2nd and higher BCP-ALL relapse post 2nd line chemotherapy (> 30% leukemic blasts in bone marrow)
- Refractory BCP- and T-ALL at 1st relapse (> 5% blasts in bone marrow after standard 2nd line induction therapy).

Specific ALL post-CAR-T cell therapy:

- 1st and higher BCP- and T-ALL relapse post autologous CAR-T cell therapy

ALL post-SCT

Inclusion Criteria

General:

- Bone marrow involvement and/or extramedullary relapse of ALL (> 30% leukemic blasts)

Specific:

- 1st and higher BCP- and T-ALL relapse post allogeneic HSCT
- 1st and higher BCP- and T-ALL relapse post-CAR-T cell therapy and post allogeneic HSCT (also without prior allo-SCT, see previous chapter)

AML

Inclusion Criteria:

- Early 1st relapse AML/ refractory disease following re-induction,
  or at least 2nd relapse AML (> 30% blasts in bone marrow or sorted blasts)

Exclusion Criteria:

- Acute promyelocytic leukemia
- Acute myeloid leukemia in patients with Down Syndrome

Soft Tissue Sarcoma

Inclusion Criteria:

- Combined or metastatic relapsed RMS,
  or first-line therapy: Progressive RMS, no option for local therapy,
  or primary diagnosis metastatic RMS in patients age > 10 years or bone/bone marrow metastasis,
  or non-resectable desmoplastic small round cell tumor (primary diagnosis or refractory/relapsed/progressive DSRCT)
- Other sarcomas

Ependymoma, Medulloblastoma and Embryonal Tumors

Inclusion Criteria:

- Medulloblastoma or ependymoma (WHO°II or III)
- Refractory or progressive disease following first-line therapy or first or multiple relapse
- Newly diagnosed ETMRs

Ewing Sarcoma

Inclusion Criteria:

- Any relapsed and/or therapy refractory Ewing sarcoma or metastatic Ewing sarcoma at the time of diagnosis.
- Tumor at biopsy accessible site, in case of metastatic disease biopsies taken from multiple sites (i.e. primary tumor and metastatic site) are welcome.

High Grade Glioma (incl. diffuse intrinsic pontine glioma)

Inclusion Criteria:

- Primary diagnosis or relapsed/progressive high-grade malignant glioma (WHO grade 3 or 4 or analogous tumors incl. DIPG)

Neuroblastoma

Inclusion Criteria:

- High risk neuroblastoma patients; any neuroblastoma relapse after high risk therapy,
  or intermediate risk neuroblastoma patients: At least second relapse after HD chemotherapy and ASCT

- Relapsed tumor accessible to low risk surgery or, in case of bone marrow infiltration and only if solid tumor tissue not available, aspirate containing at least 30% neuroblast infiltration (% after cytospin, not in bone marrow smear)

NHL

Inclusion Criteria:

- Burkitt lymphoma, mature aggressive B-cell NHL not further classified or LBL with non-response, progression, or relapse (> 40% blasts in solid Lymphoma, > 30% blasts in non-solid Lymphoma)

Osteosarcoma

Inclusion Criteria:

- Relapsed or first-line therapy refractory osteosarcoma

Rhabdoid Tumors

Inclusion Criteria:

- Relapse or first-line therapy refractory rhabdoid tumors

"Other" Refractory or Progressive/Relapsed Entities Including Rare Tumor Diseases

- Exceptional cases discussed with and agreed by INFORM Registry Trial Office
- In case of rare tumor diseases (including primary diagnosis) also with the GPOH STEP Registry
- In case of nephroblastoma, including relapse of nephroblastoma with high-risk histology (diffuse anaplasia and blast-rich subtype after preoperative chemotherapy), relapse of stage IV nephroblastoma, relapse of clear cell sarcoma (CCSK), other renal malignant tumors, and all renal cell carcinomas (RCCs)) tumors also with the respective GPOH study group.
- Primary diagnosis or relapsed/progressive of malignant endocrine tumors, including adrenocortical carcinoma (ACC), adrenocortical carcinoma of unknown origin (ACx), pheochromocytoma/paraganglioma (PCC/PGL) by SDHB or metastases, medullary thyroid cancer (MTC), neuroendocrine tumors (NETs) except appendix, with the respective GPOH study group
- In case of hepatoblastoma, retinoblastoma, or germ cell tumors with the respective GPOH study group