Frequently Asked Questions

Question How can I access the ENCR protocol?
Answer please follow this link to overview the guidelines: https://encr.eu/sites/default/files/inline-files/2021%20ECIS-IARC-EUROCARE%20call%20for%20data%20protocol_20210728.pdf

Question Is there a discrepancy regarding the recruitment of cases (study period) in page 6 vs. page 20, pertaining to the study period? "Cases must be diagnosed between 01/01/2014 – 31/12/2017" however the table has the estimated number of cases for 3 years. What is correct?
Answer There is no discrepancy. Cases must be diagnosed between 1.1.2014 – 31.12.2017, one year incidence back and forth will be considered within this 3 years window, for a registry to have a minimum of **three consecutive** years" worth of cases, providing 3 years follow-up is assured.
If you want to provide more consecutive years in the window 2014-2017 is ok but we can't pay for the further year. However, **3 years follow-up** must be assured

Question Regarding the Chemotherapy type (Preoperative Chemo/ postoperative chemo/ Both preoperative and postoperative chemo/ Chemotherapy only/ unknown) in **Neuroblastoma**, if the cases have done **only biopsy for the diagnosis**, no chemotherapy, and no surgical resection of the primary tumour what should we fill?
Answer If a case didn't have surgery or chemotherapy you should put "NO" to both variables.
If the case died and treatment was not performed therefore the answer is NO. We ask for the treatment performed and not the Intention to Treat (ITT).

Question When assigning "Relapse/recurrence" – are there any definitions and guidelines for what constitutes "recurrence" and "relapse" in this study and how these may be differentiated from "progression"?
Answer As both relapse/recurrence and progression are considered "events" in that regard (i.e., failure of first line treatment), then for this project we recommend recording relapse/recurrence/progression as a single data field with a "yes" or "no" answer (i.e., did it occur or not?). This will allow us to analyze event-free survival if we have sufficiently complete data submission on this field.
It is true that relapse and progression have different definitions, which may vary by tumour type. In general, relapse means recurrence of disease after the patient has achieved clinical remission (no evidence of disease). Tumour progression refers to either increase in size by at least 20% of the primary tumour (whilst under treatment) or new appearance of distant metastases.
We advise that the documentation of relapse or progression is done in conjunction with the registries' clinical input unless it is collected routinely already.

Question Diagnosis date of original primary follows the rule that if an event of higher priority occurs within 3 months of the date of initial diagnosis, then this should take precedence - e.g., CT scan confirms malignancy but then histological confirmation via surgery is performed within 3 months of scan – therefore, the date of surgery is chosen as date of diagnosis.
For this project, we wanted to check if date of recurrence/relapse follows the same rule as that used for recording of primary malignancy or is the date of first confirmation of recurrence/relapse used independent of the type of diagnosis event it is e.g., CT scan date recorded even if **histologically confirmed** within 3 months.
Answer For recording of date of relapse/recurrence or tumour progression, we need to recognize that relapse may often be diagnosed purely on imaging and never biopsied before second line treatment is initiated. Surgery for residual disease may occur several months after the relapse/progression occurred.
Hence, the data of relapse/recurrence of tumour progression should be recorded as **the earliest confirmed clinical date of detection** – this could be a clinical physical examination or an imaging scan or a biopsy histological result of a suspicious lesion.
Consequently, the usual Cancer Registration hierarchy for date of first diagnosis does not apply to recording date of relapse/progression. It should be noted that this hierarchy for newly diagnosed cancers does not apply to Wilms tumour treated with chemotherapy prior to nephrectomy.

Question If an imaging report, for example a CT scan states there is a differential diagnosis e.g., 'left kidney mass identified. Differential would include Wilms tumour or clear cell sarcoma' and then is confirmed histologically as a Wilms tumour- do we record the CT scan as 'positive' or 'suspicious'?
If terminology such as 'concerning for', 'suggestive of', 'possibly' etc is used for a Wilms tumour in an imaging report, but it is then confirmed histologically as a Wilms tumour, do we record the imaging as 'positive' or 'suspicious'?
Answer CT/ MRI primary site – answers refer to if the primary tumour was imaged by either CT and/or MRI, so a simple Y/N or Unknown.
CT/ MRI primary site outcome – in the scenario above, the answer relates to if there is definite evidence of a kidney tumour on imaging (regardless of histology which is confirmed in other ways) so the answer should be “positive’. Then, we move onto imaging for potential regional spread (to Lymph nodes) or distant metastases. Here we require to know what types of imaging were performed at diagnosis and if the results were conclusive (positive or negative) or only suspicious or unknown.

Question For the case of Wilms Tumour, there are a few patients who had first surgery (still searching the reason) and had total nephrectomy, then were referred to the oncology department and started the SIOP protocol. Are we filling the Stage Tier 1 after immediate surgery?
Answer Staging of renal tumours should be recorded according to the timing of nephrectomy in relation to start of chemotherapy. Even if a “SIOP” protocol was used, if the chemotherapy only commenced after nephrectomy, then stage should be recorded for an “immediate surgery” approach (i.e., do not use the “y” prefix). Tier 1 and tier 2 staging can be completed with either approach (immediate surgery or pre-nephrectomy chemotherapy). We encourage recording of tier 2 staging if the registrar has access to all the proper information (i.e., cross-sectional imaging for metastases performed prior to any chemotherapy, delay no longer than 3 weeks between surgery and referral to oncology, plus full pathology staging of the nephrectomy tumour.

Question How much time must pass from diagnosis to be able to define the tumour as a recurrence?
Answer It is not a matter of time from diagnosis but whether the patient achieved clinical remission or not before new tumours appeared at a distant site or the primary tumour showed significant enlargement (see Q4 & Q5).
Tumour progression can rarely occur within days, even during the first course of chemotherapy. Tumours can sometimes regrow rapidly after surgery before there is time to commence chemotherapy or radiotherapy. Both these scenarios are uncommon but can occur.

Question In Wilms tumour, SIOP protocol - If after chemotherapy, at surgery there is no trace of the neoplasm, is it correct to indicate it as stage y-1?
Answer Possibly, but the difference between stages y-1, y-2 and y-3 rely on the pathological report and surgical findings. In both stage y-1 and y-2, the tumour will have been completely resected with no visible residual tumour cells, even microscopically. Stage y-3 can also mean complete resection but with microscopic residue at resection margins or there may be other evidence of residual disease in the abdomen seen by the surgeon or pathologist.

Question We have a case that was confirmed both radiologically and histologically as an Extrarenal Wilms Tumour in the Retroperitoneum C48.0. Should this still be included in the project or excluded as the primary site is not C64.9?
Answer No – don't report extrarenal WT, they are not eligible as they don't meet the primary site anatomical definition in the protocol. Extra-renal WT cannot be staged according to the Toronto guidelines.

Question Are Ganglioneuroblastoma (M-9490/3) and olfactory neuroblastoma (M-9522/3) included in the neuroblastoma category in the Benchista project?
Answer Ganglioneuroblastoma (M-9490/3) is included whereas olfactory neuroblastoma (M-9522/3) isn't. The list of morphologies to be included in the project is described in the BENCHISTA Appendix.

Question If relapse/progression occurs during primary treatment is the case still suitable for inclusion in the project?
Answer Yes, if relapse/progression occurs during primary treatment the case can and should be included in the project.

Question If emergency chemotherapy commences prior to diagnosis is the case still suitable for inclusion in the project?
Answer Yes, we should include these cases and attempt to document the Toronto stage with the available investigations performed around the time of diagnosis – even if these are within a few days or weeks from emergency chemotherapy being started.
Normally in these situations the treating clinician tries to obtain all vital staging investigations as soon as possible after starting the emergency chemotherapy (which is usually indicated because of respiratory distress or other vital structure compression causing symptoms).
If there were bone metastases discovered at the first opportunity to perform a bone scan, for example, this would mean they were almost certainly already present at diagnosis. Such cases should be rare, and **we would advise the cancer registry to liaise with the clinical centre to decide if the tumour was thought to be metastatic at diagnosis or localised.**

Question For the three cancer types common in adolescents (osteosarcoma, Ewing sarcoma and rhabdomyosarcoma), are cases up to 19 years of age included in the project?
Answer Yes, for osteosarcoma, Ewing sarcoma and rhabdomyosarcoma the cases eligible are 0-19 years of age (<20 years).

Question Do we fill the laterality field only if the neuroblastoma is found in the adrenal gland?
Answer No, laterality field for neuroblastoma must be filled in any case.

Question If there is neuroblastoma found in right abdomen, then this should be recorded as right disease in the *Laterality field*?
Answer Yes, it should be recorded as right laterality.

Question If there is neuroblastoma found in thorax, head, or spinal cord, what should it be recorded in the laterality field?
Answer If the metastasis is in the same laterality as the primary site, no problem. If it has different laterality, then it must be marked as bilateral.

Question For patients with metastatic disease, i.e., right adrenal gland with metastases in liver, what should be recorded in the laterality field?
Answer For patients with metastatic disease it is necessary to mark the laterality based on the laterality of the area affected by the metastasis. In the example, the laterality would be right.

Question There is a case with histopathology confirming Mesoblastic Nephroma (M-8960/1) with pulmonary metastases, while this is rare it is documented in the literature. In our registry we would register this as Nephroma NOS (M-8960/3). Should it be included in the BENCHISTA?
Answer Regarding the coding (and hence whether the case should be included in BENCHISTA) – it needs to be considered a true "nephroblastoma" and not mesoblastic nephroma (which itself is a biologically heterogeneous entity and very much distinct from nephroblastoma). Assuming we all agree it should be coded M 8960/1, then it should be excluded from the BENCHISTA cohort.

Question I have an MRI report which states: a patient with high grade tumour in the proximal tibial metadiaphysis. The lesion extends into the subchondral region of the proximal tibia and into the knee joint. I think this would be localised tumour but because it has spread to the knee joint, I was unsure and need clarification as to whether this represents metastasis? There are no skip metastases present.
Answer This would be localised. Invasion into the knee joint would be regarded as local extension of the tumour and not metastasis.

Question We have a doubt regarding inclusion/exclusion criteria of cases in the BENCHISTA study. Should we include children from foreign countries that are treated in our country's hospitals? We are aware that the inclusion of these cases in our sample will bias our results on stage at diagnosis.

These cases usually represent more advanced stages of disease that, before accessing our national healthcare system, were assisted following clinical guidelines very different from those of our country.
Answer We only want cases diagnosed in the resident population covered by each cancer registry, so please do not include foreign children referred from other countries for treatment in your hospitals.

Question Is there a formula for the age in months at time of diagnosis and time elapsed from diagnosis to death/last follow up?
Answer We'd suggest the following: (date of diagnosis – date of birth)/30 rounded down.

Question Source used for staging: Pathological report Yes/No → We are assuming this only means reports of biopsies of suspected metastases or possible sites of metastases like bone marrow, and not the pathological reports that confirmed the diagnosis.
Answer Not totally correct – please refer to the below.

Question Is this correct or should it also be coded as yes for the original diagnostic pathology report?
Answer Yes, this should be using the pathology report of the primary tumour operation as well as including any biopsies of suspected metastases, if they occurred.

Question Primary treatment defined as given within 1 year of diagnosis: when a relapse or progression occurs within 1 year of diagnosis, we are not counting the second line therapy, just whatever happened before the event. Is this OK?
Answer Yes, it is OK to not report, if they are certain that it is second line treatment after relapse or progression.

Question We have some cases with neoadjuvant chemotherapy, surgery, then immunomodulators. Would you include this as postoperative "chemotherapy" or not?
Answer There may be some cases of neuroblastoma that have their definitive surgery "late" at the end of chemotherapy, who then only get given immunotherapy (this would be an unusual sequence). We'd like you to direct these rare cases to state "chemotherapy" as meaning a post-op systemic therapy so please in the BENCHISTA Excel File select the "Both preoperative and postoperative chemotherapy" option for chemotherapy treatment.

Question in our cancer registry we would not consider treatment given after progression as first line treatment but treatment of the progress. If this happens within a year of diagnosis, how should we proceed?
Answer The treatment given after progression should not be considered as a first line treatment even if happened within a year from diagnosis. We don't collect information on progression treatment.

Question What age limit do we use for each specific quality check indicator? Do we use age up to 20 years for bone tumors and up to 15 years for all other tumors? What about for the first indicator, DCO/autopsy among all cancer cases?
Answer Yes, please use age up to 19 inclusive (i.e., <20) for Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma and, age up to 14 (i.e., <15) for the other three tumours.
For the DCO cases is requested the number of children, so please use age up to 14 inclusive (i.e., <15).

Question In our registry, we have decided to include in the analysis an additional year (2015-2018) so we have a 4-year period. Do we report the quality checks for 3 years only or the whole period we are reporting on?
Answer Please report the quality checks for the whole period (in this case: 2015-2018).

Question Do we consider the outcome of an examination with respect to the cancer specific Toronto definition, i.e., what constitutes as a "positive" exam can differ between cancers?
Answer No, the definition of "positive" is the same for all cancers.

Question Should we include in the database a newborn with a congenital neuroblastoma that was diagnosed by autopsy just because he/she lived only for a few hours and had no chance (no time) of being diagnosed by any other method?
Answer No, you shouldn't include that case in the database.

Question We would like to clarify what you need in the quality check indicators, regarding average time to stage a patient with each disease, to provide you accurate estimates. Do you want to know the time that we need to get all the information to stage a patient or, while we have all the information necessary to perform the Toronto staging, how long do we take to stage the patient?
Answer We do want to know, once you have all the necessary information, how long it takes you to stage the patient.

Question Regarding the non-stage prognosticator FKR-PAX3 and PAX7 in rhabdomyosarcoma: in patients with a positive result for FOXO1/FKHR gene13q14 translocation (without more detailed information), should we select unknown for both FKR-PAX3 and FKR-PAX7 variables?
Answer If you have no detailed information but a patient has a positive result for FOXO1/FKHR gene13q14 translocation please select 1 for FKR-PAX3 variable.

Question Just to make sure: the abdominal ultrasound in nephroblastoma is looking for the extent of tumour spread, as the primary site imaging has already been recorded as CT/MRI. So, I have not been recording this as positive when only the primary tumour was visible, with no extension into renal and inferior cava veins, liver or lymph nodes. Is this correct?

Answer You need to record that an ultrasound was performed in column "*abdominal ultrasound*" of the database file, however in the next column "*abdominal ultrasound outcome*" it should be recorded as negative if the imaging does not show any evidence of distant metastases.

In other words, this should only be recorded as positive for distant metastases seen on ultrasound such as liver metastases or gross peritoneal metastases.

It should not be recorded as positive if the only imaging evidence for metastases is in relation to enlarged lymph nodes (which need to be confirmed histologically after nephrectomy).

Question In medulloblastoma the SCCR always coded both ICD-10 and ICD-O-3 topography as C71.6 as "standard practice" for medulloblastoma. Should we go back and change the topography to C71.9 posterior fossa when this is the reported localization?

Answer We recommend – whenever possible – to use the topographical code C71.6 which refers to the cerebellum.

The topography code for posterior fossa can be used but is classified under the general code C71.9 (brain, NOS) which means that we lose specificity. Of course, we agree that both terms are used in the context of medulloblastoma. As the primary location of the medulloblastoma is in almost all cases in the cerebellum, we would prefer use of the code C71.6.

Question Is immunohistochemical evidence enough to say the medulloblastoma belongs to the SHH subgroup when we have no molecular data?

Answer Indeed it can be and can be diagnosed by GAB and YAP stains. For trials however requires 2 methods.

Question In a case where the initial report classifies the case as either M0 or M1, but later discharge reports say M0, can we assume there has been a negative CSF result? For medulloblastoma, we still seem to be missing a lot of reports from certain hospitals.

Answer If the most recent hospital discharge report states M0, we must conclude that this has included all reports available to the clinical team and is therefore correct; probably meaning that the day 14 CSF has been done when it was not available the initial report.

Nevertheless, please ensure all quality checks are in place for the registered data. If you notice irregularities in the data provided, please ask for support from the consultant or clinician/data managers/medical source to clarify them.