Appendix

Consensus text prepared during Part 1 (DEVELOPMENT) of the project

I. Terminology and Definitions

1. Anti-cancer Modality

The type of therapy used to remove, kill, or suppress cancer cells, including:

- Systemic anti-cancer therapy (SACT; see separate definition);
- Surgery;
- Radiotherapy (including, but not limited to, external beam radiation, brachytherapy, proton beam, stereotactic radiosurgery, radioactive microspheres) but excluding radiopharmaceuticals (e.g. radioisotopes and radio-labelled monoclonal antibodies);
- Other (including, but not limited to, high-intensity focused ultrasound, cryotherapy, thermal ablation, photodynamic therapy, hyperthermia, vascular embolisation, local perfusion of SACT where there is no relevant systemic drug exposure in the opinion of the treating clinician, and anti-cancer agents not meeting the definition of SACT).

Note: Since radioisotopes such as sodium iodide (I-131) used for thyroid carcinoma, and radio-labelled monoclonal antibodies such as lutetium dotatate (Lu-177) used for gastroenteropancreatic neuroendocrine tumors have systemic effects, they are included in the definition of SACT, rather than radiotherapy, which has mainly loco-regional effects.

2. Clinical progression of disease (cPD)

The clear worsening of the patient's clinical state due to malignancy, in the opinion of the treating clinician, taking into consideration clinical findings, +/- appearance/deterioration of clinical signs, +/- symptoms, +/- laboratory results, +/- imaging (including, but not limited to, objective imaging response criteria).

Note: Objective imaging response criteria include RECIST and/or other generally accepted guidelines. The clinician should align cPD where possible with the definition of progressive disease (PD) by objective imaging response criteria. The diagnosis of cPD would usually necessitate administration of a different anti-cancer therapy (systemic, locoregional or both) or best supportive care alone.

3. Clinical setting

The maximum extent of cancer spread to date, and in the opinion of the treating clinician denoted as

A: Early setting;

B: Locally advanced setting;

C: Metastatic setting.

Note: The treating clinician should take into consideration TNM staging, type of cancer, surgical resectability or otherwise, and/or other clinical features.

4. Intolerability

Significant toxicity in any organ system, and/or adverse physical, social, psychological or emotional experience(s) occurring as a result of systemic anti-cancer therapy (SACT), that adversely impacts the patient's quality of life and leads to discontinuation of the SACT.

5. Systemic anti-cancer agent

A (bio)pharmaceutical product used for the systemic treatment of malignant disease, including — but not limited to — cytotoxic, endocrine, targeted, immunotherapy, cell & gene therapy, and radiopharmaceuticals (e.g. radioisotopes and radio-labelled monoclonal antibodies) irrespective of route of administration, that has been approved by one or both of the EMA and the US FDA for treatment of any type or stage of cancer, and where the intent is to obtain a systemic (rather than a purely local/regional) effect.

Note: A clinical substitute (CS) is another systemic anti-cancer agent that would usually have a similar chemical structure, biological target(s), and biological effect(s) to the agent that had been intolerable, with a similar or different toxicity profile. In the opinion of the treating clinician, the new agent would not usually be used had there been cPD whilst receiving the intolerable agent, and the new agent is expected to result in a similar benefit to the patient as the intolerable agent.

A systemic anti-cancer agent in clinical development not yet approved by one or both of the EMA and the US FDA for treatment of any type or stage of cancer (as on date of starting such therapy) should be termed an 'experimental systemic anti-cancer agent'.

A systemic anti-cancer agent refers to a single (bio)pharmaceutical product. On the other hand, systematic anti-cancer therapy (SACT), defined below separately, may consist of a single or multiple systemic anti-cancer agent(s).

6. Systemic anti-cancer therapy (SACT)

An individual SACT has the following features:

· It consists of one or more systemic anti-cancer agents, which can be administered alone or in combination or sequence (which might include alternating, hybrid, continuation maintenance therapy and/or switch-maintenance therapy);

· It is prospectively planned, with any change in the components not determined by response to treatment or toxicity;

· It is usually (but not necessarily) administered in repeating cycles;

· It is administered systemically, or via local/regional routes but with the intention of systemic effect or control of overall tumour burden;

· It is given at a clinically relevant dose for a duration that is expected to exert systemic anti-cancer effect.

Note: SACT may be "Approved" or "Experimental";

"Approved" SACT contains at least one anticancer agent approved by one or both of the EMA and the US FDA for treatment of any type or stage of cancer (as on date of starting such therapy); it may also contain one or more experimental anti-cancer agent(s);

"Experimental" SACT is comprised exclusively of experimental anti-cancer agent(s) (as on date of starting such therapy);

A patient participating in a blinded randomized clinical trial where the control arm consists only of a placebo should not be considered to have received a SACT in that trial unless unblinded information is available;

When a patient has two (or more) cancer diagnoses, a SACT administered for one cancer should not be considered a SACT for the other cancer(s), unless it is also considered effective against the other cancer(s);

An anticancer agent that is approved by one or both of the EMA and the US FDA for a given cancer but used with the intention of providing only supportive/symptomatic care (but not direct anti-cancer effect) for another cancer (e.g., dexamethasone is approved for multiple myeloma, but may also be used to prevent nausea and vomiting in patients with other cancers) should not be considered as an SACT for that other cancer.

7. Line of Therapy (LoT)

A serial chronological number assigned to each systemic anti-cancer therapy (SACT) administered to a patient that denotes a discrete attempt to treat the cancer.

8. Treatment intent

Treatment intent, in the opinion of the treating clinician, can be curative or non-curative; the latter can be potentially life-extending or palliative.

Curative therapy aims at elimination of cancer and preventing its recurrence. Non-curative therapy aims at maintaining or improving one or both of quality and quantity of life (i.e. inducing "remission") but without the expectation of cure.

II. Which treatments should be assigned a line of therapy?

The current ESMO project will be limited to systemic therapies only. A future project by the same working group will consider if lines of therapy should be assigned for local/loco-regional therapies.

III. Proposed standardised format for reporting lines of therapy

Total Systemic LoT is reported in the format **[cLoT + ncLoT] + eLoT**

Note: cLoT is the number of SACT administered with curative intent and/or in the early clinical setting.

ncLoT is the number of SACT given with non-curative intent and/or in the locally advanced or metastatic clinical setting. cLoT and ncLoT contain at least one anticancer agent approved by one or both of the EMA and the US FDA for treatment of any type or stage of cancer as on date of starting such therapy; it may also contain one or more experimental anti-cancer agent(s).

eLoT is the number of "experimental" SACT administered in any clinical setting (early, locally advanced, metastatic). "Experimental" SACT is comprised exclusively of experimental anti-cancer agent(s) as on date of starting such therapy.

While assigning LoT, the treatment intent (i.e., curative or non-curative) should be the primary consideration, and clinical setting (i.e., early, locally advanced, or metastatic) the secondary consideration.