

Europe's Beating Cancer Plan – the endocrinology perspective

The European Society of Endocrinology (ESE) applauds the strong focus of the European Commission on Cancer. The **interaction between cancer and the endocrine system** is complex and relates to the action of hormones like estrogens, androgens, insulin, and others. There are four significant ways in which the endocrine system relates to cancer:

1. obesity has been identified as an independent risk factor for many cancers. **Nearly 40% of all cancers can be attributed to overweight and obesity**, and in particular endometrial, postmenopausal breast and colorectal cancer – all related to the endocrine system – account for over 60% of all cancers attributed to obesity
2. environmental factors like **Endocrine Disrupting Chemicals (EDC)** have an effect on different hormones and affect both the development of obesity and cancer¹
3. certain **endocrine cancers** are on the rise, e.g. thyroid (> 50 000 new cases per year) and neuro-endocrine tumours (NET). More than 100 000 EU citizens have been diagnosed with NET, 60% at a late stage, which is impacting the outcomes of these cancers
4. the endocrine system is **vulnerable to aggressive anti-cancer treatments** that result in endocrine comorbidities in cancer survivors.

The European Society of Endocrinology encourages the EU to take into account the endocrine system in all facets of the Beating Cancer plan, as the endocrine system influences and is influenced by cancer prevention, treatment and post-treatment care.

In response to the European Commission's roadmap on the Beating Cancer Plan, ESE has four main remarks:

- Prevention measures need to become a focus area
- European Reference Networks have a key role in early detection and diagnosis
- National Action Plans should address comorbidities
- A pan-European and comprehensive approach to cancer and beyond is needed

ESE agrees that prevention measures need to become a focus area

The **obesity pandemic is a major driver of cancer incidence**. A recent population-based cohort study of 2.3 M adolescents shows that adolescent obesity is linked to cancer risk in midlife². Also, there is a clear trend that obesity related cancers are being diagnosed increasingly at younger ages³.

Acknowledging that two thirds of cancer cases cannot be prevented by modifying lifestyle and diet, other obesity prevention strategies must be stepped up to reduce cancer incidence and mortality. While ESE advocates for more research on the contributing factors, more specialized health care structures to tackle obesity as a severe disease are also needed. Obesity prevention needs to start at the level of pregnant

¹ Jeffrys et al, Int J of Cancer 2004, vol 112, p348-351

² Furer A, Lancet Diabetes Endocrinol.2020 Mar;8(3):216-225)

³ Berger NA, Obesity 2018: 26, 641-650

mothers, childhood and be carried forward into adult life. National and Community based action plans to secure lower calorie intake and reduction of sugar consumption have proven their benefit.

The **link between Endocrine Disrupting Chemicals (EDCs) and cancer** is subject of many studies, including those on breast cancer⁴ and testicular cancer⁵. ESE supports that more research needs to be commissioned and funded, and that a strong legislative framework needs to be put in place, strictly following the precautionary principle, to avoid pesticides, biocides or consumer products containing suspected EDCs to be further used⁶. Public awareness campaigns around practical ways to reduce the exposure to EDCs in everyday life are needed.

The Green Deal needs to spend appropriate attention to the risks imposed by EDCs. New legislation, including criteria under chemicals legislation REACH, is needed to reduce the exposure of EU citizens to EDCs.

European Reference Networks have a key role in early detection and diagnosis

In the area of **endocrine cancers**, ESE posits that more efforts are needed to fully understand the epidemiology and clinical data. This applies a.o. to the area of thyroid and rare endocrine cancers, that have been understudied and under-invested, as demonstrated by the low number of viable treatment options and late diagnosis at an advanced stage.

It is important to improve early detection and diagnosis of endocrine cancers, often presenting in children and young adults. ESE subscribes that ERNs like endo-ERN and EURACAN are the structures to address this and that they can, provided sufficient resources are made available and in close collaboration with scientific societies, secure that the information obtained is turned into broadly supported clinical guidelines, and into educational curricula.

Effective treatment and care in rare disease cancers also needs innovation. The expansion of existing therapies towards these rare diseases needs to build on quality evidence gathering in the context of international collaboration. Several structures exist already that, if better supported, provide the platform to do this (ERNs, European Society of Neuro-Endocrine Tumours - ENETS, European Network for the Study of Adrenal Tumours ENS@T, European Thyroid Association ETA) a.o..

Altogether these improvements in diagnosis and therapy will impact on the life of patients with rare cancers.

National Action Plans should address comorbidities

ESE points to the need for an ongoing and multidisciplinary approach towards **cancer survivors**.

Often aggressive cancer interventions result in important **hormone related co-morbidity** as the endocrine system is especially sensitive. Endocrine sequelae of cancer therapy include functional alterations in hypothalamic-pituitary, thyroid, parathyroid, adrenal and gonadal regulation, as well as bone, obesity and metabolic complications⁷. Recently introduced cancer immunotherapies are a common cause of endocrine

⁴ Rodgers et al, *Environmental Research* 160 (2018) 152-182]

⁵ Skakkebaek et al *Physiol Rev* 2016 (55-97).

⁶ Nature Reviews Jan 2020: Consensus on the key characteristics of Endocrine Disruptors as a basis for hazard identification

⁷ Gebauer et al, *Endocr Rev.* 2019 Jun 1;40(3):711-767. Long term endocrine and metabolic consequences in survivors of childhood cancer a systematic review

auto-immunities. Following irradiation, endocrine organs like the thyroid are at risk for subsequent malignancies.

Cancer survivors require lifelong care to address the potential comorbidities linked to their cancer or the therapies they were exposed to. Of particular attention is the impact of these substances on the endocrine system, relating to issues with development of infertility, obesity, metabolic syndrome and cardiovascular co-morbidities. National Action Plans to turn scientific and clinical data into a well-supported and funded health care provision are needed.

The development of a European Cancer Knowledge Research Centre requires a multidisciplinary approach. An important task is at the level of the EU Joint Research Centre to develop authoritative guidelines to address the cancer challenge.

A pan-European and comprehensive approach to cancer and beyond is needed

ESE agrees that the complex nature of cancer, the level of research that needs to be undertaken and the funding required is only possible when pooling national and European experts, laboratories, a pan-European data space approach and a strong engagement of industry, whose international nature and research power needs to be a major contributor to the success of the Beating Cancer Plan.

ESE supports the broad consultative approach outlined in the Commission's roadmap. In addition to consulting cancer expert groups, ESE encourages the Commission to consult extensively with expert groups beyond the focus area of cancer alone. As outlined in the introduction, endocrinology relates to cancer not only because of the existence of endocrine cancers, but also with regard to broader disease groups like obesity, environmental factors such as endocrine disrupting chemicals, and the reactions of the endocrine system to cancer treatment. ESE can provide technical expertise on a wide range of topics that contribute to a better understanding of cancer.

For more information, contact:

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