GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

THE ESMO-ECPC GUIDE ON SURVIVORSHIP

ECPC Annual Meeting, Bruxelles 17.6.2017
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CHEM, Esch, LU
ESMO Practising Oncologists' Working Group
ESMO Educational Steering Committee

WHO IS A CANCER SURVIVOR?

- Only someone who has been **cured** from cancer?
- Also someone who lives in a ***long*** remission (without evidence of remaining disease)? (how long is long??)
- Also someone with remaining but stable and **quiescent** cancer (without treatment)?
- Also someone under **maintainance treatment**? Even though going on for years??….
- Only after 2 years of follow-up??

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CANCER SURVIVOR ACCORDING TO WIKIPEDIA

A cancer survivor is a person with cancer of any type who is still living.

Whether a person becomes a survivor at the time of diagnosis or after completing treatment, whether people who are actively dying are considered survivors, and whether healthy friends and family members of the cancer patient are also considered survivors, varies from group to group. (NCI and NCCS definitions similar)

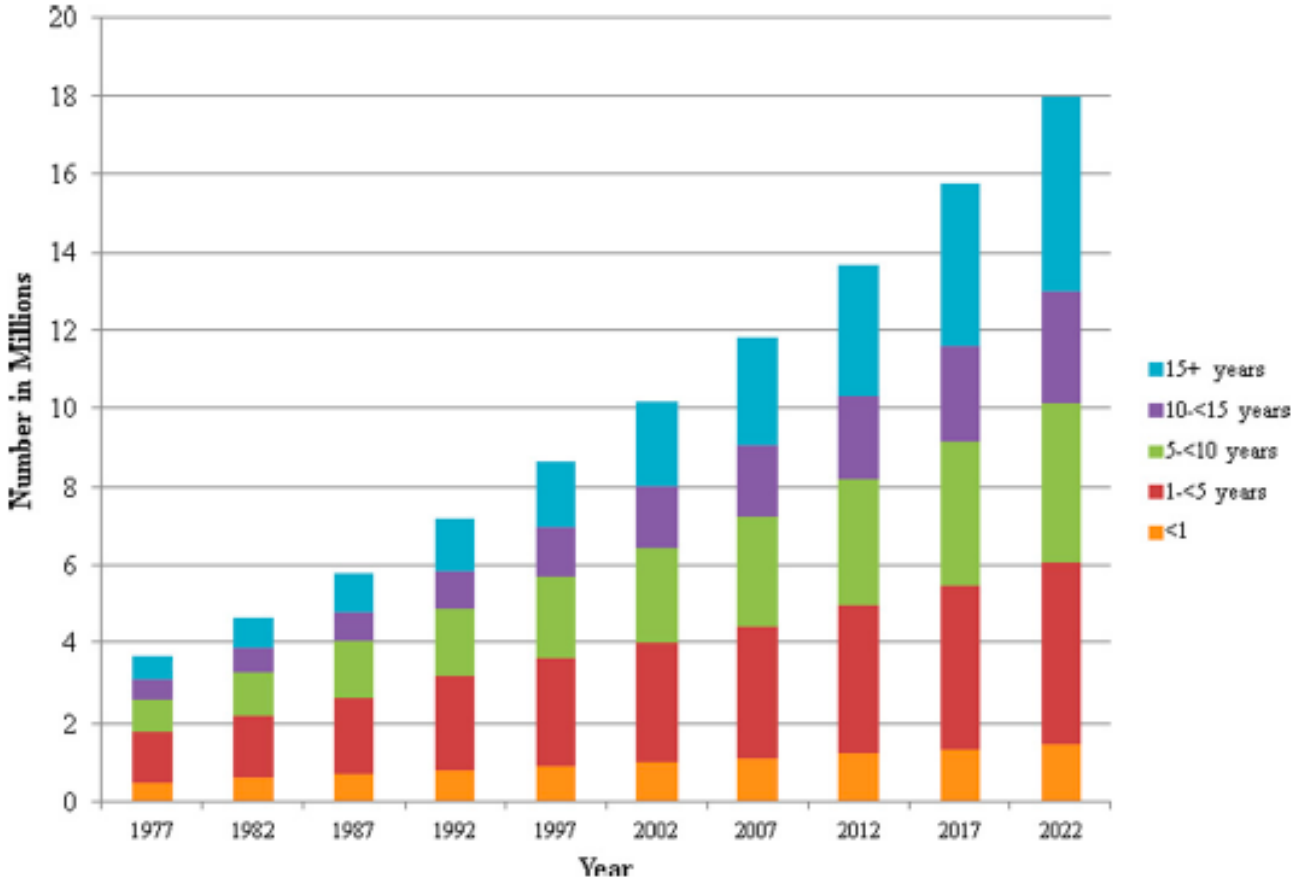
Macmillan Cancer Support in the UK defines a cancer survivor **as someone who is "living with or beyond cancer",** namely someone who:

has completed initial cancer management and has no apparent evidence of active disease;

is living with progressive disease and may be receiving cancer treatment, but is not in the terminal phases of illness; or

has had cancer in the past.

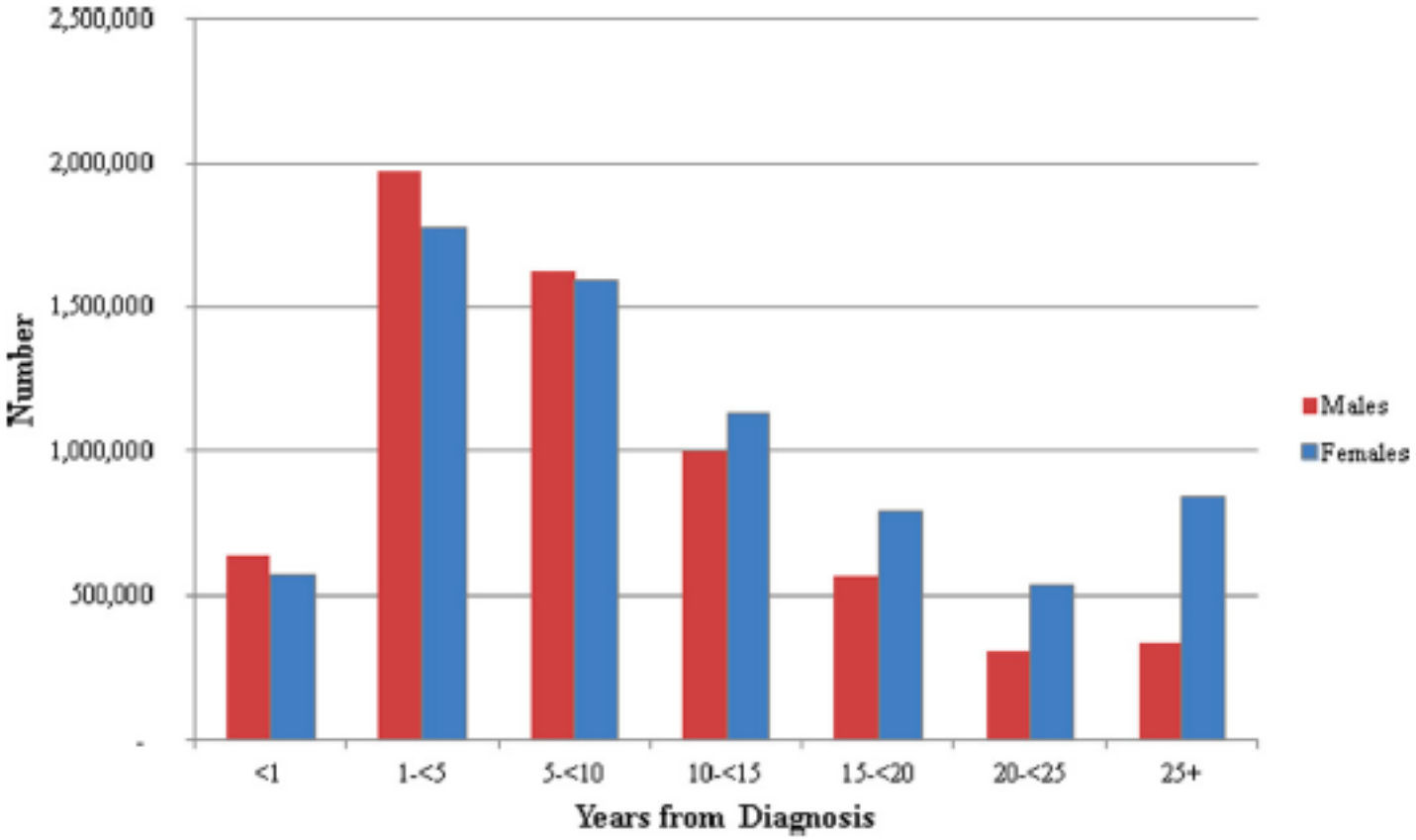
CANCER SURVIVORS – RISING!



Estimated and projected number of cancer survivors in the United States from 1977–2022 by years since diagnosis.

De Moor, *et al.* Cancer Survivors in the United States: Prevalence across the Survivorship Trajectory and Implications for Care; Cancer Epidemiol Biomarkers Prev. 2013 Apr; 22(4): 561–570.

FOLLOW-UP: 25 YEARS AND MORE

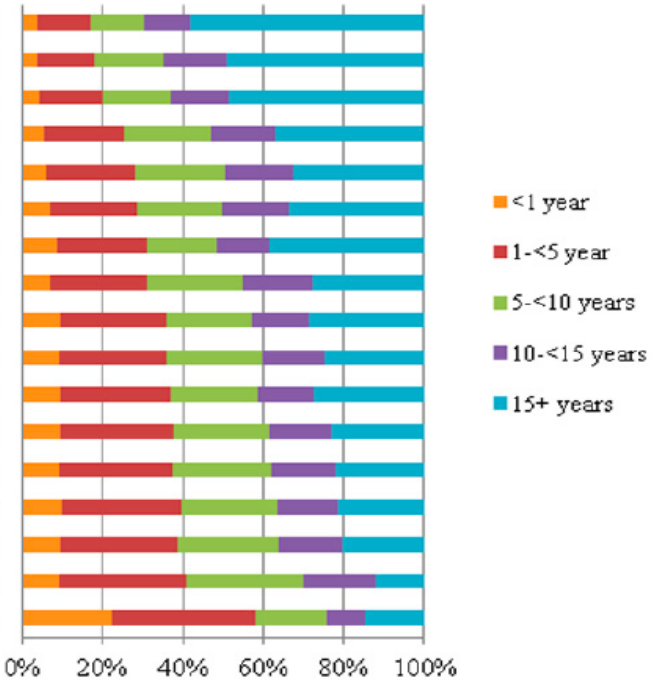


Esimated number of cancer survivors in the United States as of January 1, 2012 by time since diagnosis and sex.

De Moor, *et al*. Cancer Survivors in the United States: Prevalence across the Survivorship Trajectory and Implications for Care; Cancer Epidemiol Biomarkers Prev. 2013 Apr; 22(4): 561–570.

SURVIVORSHIP VARIES BY CANCER TYPE (AND OVERALL MORTALITY FACTORS)

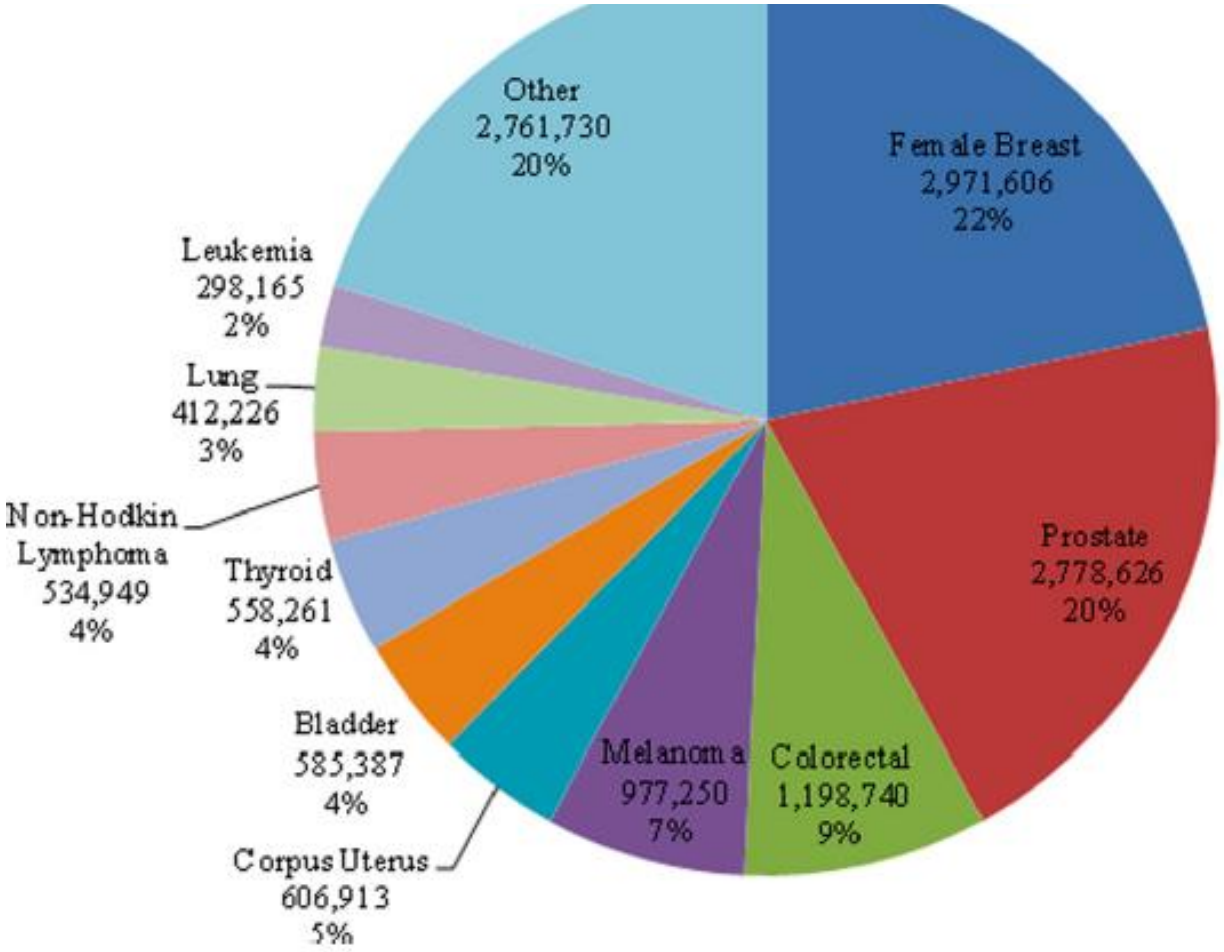
5-Year Survival Rates[1]	Median age at Diagnosis[1]	Cancer Site
67.9	48	Cervix
95.2	33	Testis
84.7	38	Hodgkin
97.5	50	Thyroid
91.2	61	Melanoma
82.7	61	Corpus
43.7	63	Ovary
88.9	61	Breast
55.0	66	Leukemia
65.4	66	All sites
61.5	62	Oral Cavity
64.3	69	Colorectal
77.7	73	Bladder
68.2	66	NHL
70.6	64	Kidney
99.2	67	Prostate
15.9	70	Lung



[1]Howlader N, Noone A, Krapcho M, Neyman N, Aminou R, Waldron W, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA. SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). Bethesda, MD: National Cancer Institute based on November 2011 SEER data submission, posted to the SEER web site, April 2012.

Estimated number of cancer survivors in the United States as of January 1, 2012 by cancer site and years from diagnosis.

US: >10 MILLION CANCER SURVIVORS IN 2012



Estimated number of cancer survivors in the United States as of January 1, 2012 by cancer site.

De Moor, *et al.* Cancer Survivors in the United States: Prevalence across the Survivorship Trajectory and Implications for Care; Cancer Epidemiol Biomarkers Prev. 2013 Apr; 22(4): 561–570.

A DAY IN MY LIFE CONSULTING A CANCER SURVIVOR IN 1999

- Happy to see my patients survive as responders to treatment
- Establish follow-up plans for medical exams (mammographies, CT- scans, endoscopies), often in a « copy-paste » 3 monthly style (due to the lack of evidence based guidelines)
- Deal more and more with other diseases (i.e. diabetes, etc..) as the follow-up continues (or refer for any of these to the GP)
- Refer to a psychologist in case of anxiety or reactional depression problems

SURVIVORSHIP CARE IS A LOT MORE

- Personalised follow-up plan *including secondary prevention features*
- Coping with ongoing disease and treatment related side effects and sequelae
- Coping with compliance in maintainance treatments
- Trying to rehabilitate: getting body and mind back in shape
- Trying to re conciliate: social life, both within the family and in the community
- Trying to re integrate: workplace, financial burdens
- Dealing with uncertainty: how long will remain a cancer survivor

DIFFERENT GROUPS OF CANCER SURVIVORS

- Patients having completed their treatment (in follow-up)
- Patients undergoing preventive anti cancer treatment (i.e. 5-10 y Tamoxifen in breast or LH-RH agonists in prostate cancer)
- Patients undergoing extended therapy to maintain disease control (CML)
- Patients undergoing prolongefd treatment for advanced/metastatic disease (i.e. monoclonals in Her2 metastatic breast cancer)

CANCER SURVIVORSHIP RESEARCH: DEFINITION

- Although definitions vary, cancer survivorship care and research is widely viewed as
- **focusing on the health and life of a person with cancer beyond the acute diagnosis and treatment phase**. According to the National Cancer Institute's Office of Cancer Survivorship, research in this area seeks to
- **"prevent and control adverse cancer diagnosis and treatment-related outcomes**..., to provide a knowledge base regarding **optimal follow-up care and surveillance** of cancers, and to optimize health after cancer treatment."

Jacobsen P, *et al.* ASCO Annual Meeting 2017 Educational Book, 674-83

SURVIVORSHIP
Evolution of Survivorship Science in Europe

- Rowland JH, *et al.* **Cancer Survivorship Research in Europe and the United States: Where have we been, where are we going, and what can we learn from each other?** Cancer 2013; 119(0 11):2094-2108.
- Understanding the evolution of cancer survivorship within the context of different political and healthcare systems is important for identifying the future steps…
- Europe is a complex grouping of 50 countries with >700 million inhabitants, marked cultural, economic and societal variations, and significant variation in the models and levels of health and social welfare provision.
- Not surprisingly, the field of cancer survivorship research has followed a somewhat different trajectory in Europe. In contrast to the US, in Europe the term “cancer survivor” is used less often by individuals with a cancer diagnosis. In the European medical literature, this term is typically applied to cancer patients surviving tumor-free at least five years after their diagnosis…

and we wanted to change it !

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THE ESMO-ECPC GUIDE ON SURVIVORSHIP

Approaching the needs of patients in a curable or chronic disease state

PATIENT GUIDE IN SURVIVORSHIP

Task Force: Nikolaos Mitsimponas, Stefan Rauh, Francesco Florindi, Svetlana Jezdic




Editorial group

ECPC: Francesco De Lorenzo, Kathi Apostolidis, Francesco Florindi

ESMO: Nikolaos Mitsimponas, Stefan Rauh, Georges Pentheroudakis, Svetlana Jezdic, Jean-Yves Douillard, Claire Bramley, Malvika Vyas, Francesca Longo

Initiated as a part of ESMO Patient Guides series by the Guidelines Committee.

Kick-off meeting during the ESMO 2016 Congress in Copenhagen, thereafter a number of TCs and e-mail exchanges within Task Force.

Plan to involve reviewers from the EONS and IPOS.

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TARGET: PATIENTS SUBJECT TO SURVIVORSHIP CARE

All cancer patients having absolved their first active anti cancer treatment

GUIDE IN SURVIVORSHIP

Definition of survivorship

Survivorship is the pathway in the fight against cancer, which is focused on health and the physical, psychological and economic issues of the life of people after the end of the initial step of treatment. This experience refers to people having no disease after finishing treatment, to people who continue to receive treatment to reduce the risk of the cancer coming back and to people with asymptomatic or well controlled disease, who receive treatment to manage chronic disease. Survivorship includes issues related to the follow up care, the management of late effects of treatment, the improvement of the life quality and the psychological and emotional support. Family members, friends and caregivers should also be considered as part of the survivorship.

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SURVIVORSHIP

Unique and ongoing experience for each person

What really matters is to find strength and the best way go through initial and continuing difficulties and to regain as much as possible the aspects of life before cancer.

Life is different after cancer

I appreciate the little things of the life

I appreciate life more

I have greater self acceptance

I feel anxious that cancer will come back

I feel more anxious about my health

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GUIDE IN SURVIVORSHIP

Content list

Support to cope with the new reality - Who can help me?

Life after initial treatment - How can I regain my normal life back?

Preventive Health - Improve Lifestyle - Are there things to do?

Follow-up care

Comorbidities and management of comorbidities

Keeping a personal health record / Survivorship care plan

Survivorship dictionary

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GUIDE IN SURVIVORSHIP

Support to cope with the new reality - Who can help me?

Cancer rehabilitation

Patient support groups

Psychological support of the patient and his/her family

The role of healthcare professionals (oncologist, general practitioner, oncology nurse)

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GUIDE IN SURVIVORSHIP

Follow-up care

Detection and management of treatment- or tumor-related symptoms
Chemotherapy induced nausea and vomiting
Pain and peripheral neuropathy
Bone loss with the possibility of subsequent osteoporosis
Mucosal, dental and soft tissue problems
Skin toxicity
Lymphoedema
Heart problems and drug-induced cardiac toxicity
Chronic fatigue
Sleep disorders
Emotional difficulties, Anxiety, Depression, Loss of self confidence and self esteem
Cognitive Function - “Chemo Brain”
Eye problems
Hormone (endocrine) system problems - sexual dysfunction, premature menopause, infertility
Impotence and lack of libido
Urological problems
Gastrointestinal problems, digestion
Lung problems
Prevention and detection of cancer recurrence
Prevention and early detection of new primary cancers for patients and their family members
Secondary cancers
Hereditary cancers

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GUIDE IN SURVIVORSHIP

Life after initial treatment - How can I regain my normal life back?

Perspective and self confidence

Changes in family and relationships

Your sexual life & becoming a parent

Returning to work, finding new hobbies and interests

Managing your finances

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GUIDE IN SURVIVORSHIP

Preventive Health - Improve Lifestyle - Are there things to do?

- Healthy lifestyles
  - Physical activity
  - Nutrition and weight management
  - Stress management
- What to prevent
  - Reducing alcohol consumption
  - Smoking cessation
  - Avoidance of excessive exposure to UV-radiation
  - Avoid worsening side effects through the use of specific drugs
  - Infections and vaccinations

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GUIDE IN SURVIVORSHIP

Further content list

Comorbidities and management of comorbidities

Keeping a personal health record / Survivorship care plan

Survivorship dictionary

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GUIDE IN SURVIVORSHIP

Insight into survivorship plan

Survivorship check list, care plan and treatment summary

Background information

Family history of cancer Yes ☐ No ☐

Genetic/hereditary risk factor, predisposing conditions: ..... (free lines) .....

Genetic counseling Yes ☐ No ☐

Genetic testing results: ..... (free lines) .....

Diagnosis

Cancer type and location: ..... (free lines) .....

Date of diagnosis(year): .....

Radiation therapy: Yes ☐ No ☐

Radiation date: .....

Radiation area: Chest ☐ Abdomen ☐ Pelvic area ☐ Head ☐

Neck ☐ Testis ☐ Breast and Axilla ☐

Other area (i.e. extremities) ☐

Systemic therapy (Chemotherapy, hormonal therapy, immunotherapy, targeted therapies): Yes ☐ No ☐

Type of therapy: Chemotherapy ☐ Hormonal therapy ☐

targeted therapies ☐ Immuntherapy ☐

Combination ☐

Psychological and social aspects in survivorship:

Psychological support: Family ☐ Friends ☐

Cancer support groups ☐ social workers ☐

Health care professionals ☐ other ☐

Rehabilitation Program: Yes ☐ No ☐

Duration of rehabilitation program: .....

Changes in family relationships: ..... (free lines) .....

Changes or difficulties by returning back to work: ..... (free lines) .....

SCHEDULE OF FOLLOW UP VISITS

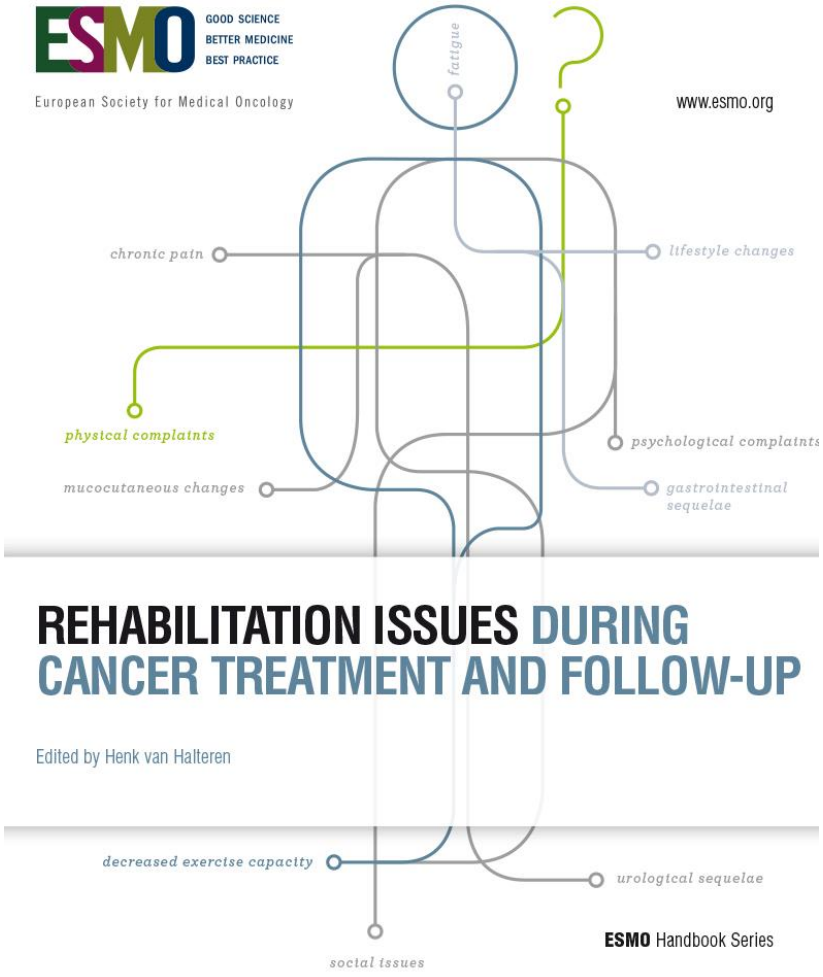
Doctor's name	Time of visit

SURVEILLANCE CLINICAL EXAMINATION AND FOLLOW-UP IMAGING AND LABORATORY TESTS:

Test/Examination	When	Results

ESMO EDUCATION COMMITMENT

Survivorship



- Sessions at ESMO events for medical professionals and patient advocates
- A title in Handbook series
- A dedicated section in Curriculum for training in medical oncology
- A dedicated chapter in each of ESMO Clinical Practice Guidelines

ESMO GUIDELINES

Evolution from follow-up to follow-up, long term implications and survivorship

as part of the initial presentation of disseminated DLBCL [49]. In comparison with CT scan, MRI better defines the local extent of the disease and cortical changes. An adapted staging system for PBoL has been proposed by the IELSG (Table 6) [13, 50].

The prognosis of primary bone DLBCLs mainly depends on the disease extent: 5-year OS rates vary from >80% for stage IE to <40% for disseminated DLBCL with bone localisation [51]. The role of the IPI in predicting prognosis of primary DLBCL of the bone seems limited [13, 49, 51].

treatment. Primary bone DLBCL should be treated with anthracycline-containing chemotherapy regimens together with rituximab, although the benefit of the addition of rituximab has not formally studied specifically in the subset of patients with PBoL. The role of consolidation RT is not well defined because the available data are very controversial and mainly come from retrospective analyses that suggest benefit [51, 52]. Indeed, R-CHOP ± consolidation RT remains the standard approach for the patients with any stage of DLBCL with bone involvement [III, B]. Whether RT to sites of bone involvement is truly needed or can be spared (at least in cases with a negative PET scan after chemoimmunotherapy) should be addressed in appropriately designed prospective randomised trials [51]. When consolidation RT is given to localised lesions, there is

detectable upon CT scan. PET scan is mandatory in response assessment as in nodal DLBCL; however, residual PET uptake can persist and may resolve slowly, representing bone healing rather than active disease. New treatments such as HDCT/ASCT or alternative chemoimmunotherapy are only recommended in the case of biopsy-proven persisting disease or clear clinical or radiological progression [III, A].

Finally, long-term bone health preventive measures should also be taken into account in patients with PBoL, including evaluation and treatment of any underlying osteoporosis, and/or vitamin D deficiency.

follow-up

Follow-up monitoring is not different from that of nodal DLBCL [1].

personalised medicine

There are still many open issues in the treatment of extranodal DLBCL. New agents targeting distinct molecular pathways involved in disease pathogenesis are in progress and are being tested in ongoing trials. So far, none of these agents is appropri-

Table 7. Levels of evidence and grades of recommendation (adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System[a])

Levels of evidence	
I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, experts opinions
Grades of recommendation	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, …), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

[a]By permission of the Infectious Diseases Society of America [100].

personalised medicine

Progress in the diagnosis of ALL with identification of genomic-defined sub-entities, the evaluation of MRD, and new targeted therapies have led to a substantial realisation of personalised medicine in adult ALL. Current options such as less intensive chemotherapy, new modalities of SCT, incorporation of targeted therapies and optimal combinations of treatments require prospective, cooperative research, hereby further refining the individualised approach to each patient.

follow-up and long-term implications

The follow-up of asymptomatic patients should include blood cell counts and routine chemistry during maintenance therapy; usually every 2 weeks during the first 2 years to adjust treatment accordingly. Thereafter, follow-up should be 3-monthly during years 1, 2 and 3, since the majority of relapses occur within the first 2.5 years after initiation of treatment; then half-yearly until the end of the 5th year. For evaluation of MRD, which is now the most important prognostic parameter, bone marrow aspirations are required 3-monthly. It is also desirable in Ph+ MRD (BCR-ABL) and, if possible, for mutations to another TKI inhibitor.

In adults, adverse long-term effects are fewer compared to children with ALL, and most adult ALL patients are cured. Clinical conditions. Relevant late toxicities are: endocrine disorders (thyroid, gonadal), osteonecrosis/osteoporosis and mucosal disorders, cataract, cardiovascular disorders, infection, graft versus host disease/sicca syndrome, fatigue, cognitive disorders. Second malignancies can also occur

patients receiving proteasome inhibitor-based therapies [4]. i.v. immunoglobulin prophylaxis is not routinely recommended [4].

to identify molecular markers which could lead to advances in personalised medicine.

Renal failure

Bortezomib-based therapies (in combination with dexamethasone ± thalidomide or doxorubicin or cyclophosphamide) is the treatment of choice in patients with renal failure [II, B] [4, 47]. Other proteasome inhibitors are under investigation. The use of

Follow-up, long-term implications and survivorship

Full blood count, serum and urine electrophoresis and/or serum-FLC determination, creatinine and calcium should be carried out

Annals of Oncology Clinical Practice Guidelines

Table 7. Summary of recommendations

The diagnosis of MM must include the criteria updated in 2014 by the International Myeloma Working Group.
Immediate treatment is not recommended for patients with indolent myeloma.
For patients < 70 years in good clinical condition, induction followed by high-dose therapy with ASCT is the standard treatment.
For relapsed/refractory MM, the most commonly used regimens are proteasome inhibitor- or lenalidomide-containing regimens. New triplet combinations are increasing PFS.
In advanced cases, pomalidomide plus low-dose dexamethasone and daratumumab are approved.

ASCT, autologous stem cell transplantation; PFS, progression-free survival; MM, multiple myeloma.

Methodology

These Clinical Practice Guidelines were developed in accordance with the ESMO standard operating procedures for clinical practice guidelines development http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology. The relevant literature has been selected by the expert authors. A summary of recommendations is shown in Table 7. Levels of evidence and grades of recommendation have been applied using the system shown in Table 8. Statements without grading were considered justified standard clinical practice by the experts and the ESMO Faculty. This manuscript has been subjected to an anonymous peer review process.

Disclosure

PM has reported advisory boards and honoraria from Celgene, Janssen, Takeda, Amgen and Novartis; JSM has reported advisory

ESMO

ESMO / ASCO Recommendations for a Global Curriculum in Medical Oncology

Edition 2016

ESMO Open
Cancer Horizons

9. SURVIVORSHIP	
by Elizabeth Charlotte Moser, Charles L Shapiro and Lifang Liu	
Objectives	• To be able to perform outpatient follow-up assessments based on best practice or guideline recommendations for the detection of cancer recurrence, new primary cancers and to evaluate the signs and symptoms of longterm and late side effects of either the cancer or its treatment • To be able to educate patients, families, caregivers and primary care providers about: ◦ the familial, socioeconomic and lifestyles that may increase the risks of cancer recurrence or new primary cancers ◦ the importance of developing and/or maintaining physically active lifestyles, weight management and avoidance of obesity, reducing alcohol consumption, tobacco cessation, making healthy dietary choices, managing depression/anxiety ◦ financial/back to work issues, and to successfully reintegrate into a productive social and professional life
Awareness	• Awareness of the existence of different roles of follow-up: ◦ Screening for cancer recurrence and second primary cancers ◦ Management of long-term and late side effects: mental/physical/socioeconomic ◦ Family and lifestyle risk evaluation, including adverse health behaviours and interventions dedicated to promote healthier lifestyles ◦ Empowerment among patients and patients' advocates

9. SURVIVORSHIP	
by Elizabeth Charlotte Moser, Charles L Shapiro and Lifang Liu	
Awareness *(continued)*	• Awareness of the existence and risks of treatment-related problems including: ◦ Chronic fatigue ◦ Pain, disabling neuropathy ◦ Skin, mucosal and dental problems ◦ Second primary cancers (treatment-related, genetics-related or developing as the population ages) ◦ Cardiovascular risk and early symptoms such as hypertension and shortness of breath ◦ Cognitive dysfunction ◦ Urological problems ◦ Gastrointestinal problems ◦ Changes due to cancer treatment, including premature menopause, bone loss with the possibility of subsequent osteoporosis, infertility, impotence and sexual dysfunction ◦ Anxiety, depression and loss of self-esteem and confidence ◦ Relational, social and financial impact (eg, retention to, resume work, inaccessibility to insurance and mortgages)

9. SURVIVORSHIP	
by Elizabeth Charlotte Moser, Charles L Shapiro and Lifang Liu	
Awareness *(continued)*	• Awareness of the signs or symptoms of cancer recurrence or treatment-related side effects and the use of diagnostic imaging modalities as indicated by best practice or guideline recommendations including: ◦ Thorough investigation of new or persistent symptoms as clinically indicated ◦ Indications for screening including imaging modalities and blood tests based on the primary cancer ◦ The screening, detection and treatment of anxiety, depression, suicidal tendency and socioeconomic problems ◦ The recognition that some new cancers and medical problems will occur in the course of normal ageing and that cancer survivors should receive routine standard preventative health maintenance (eg, immunisations, preventive screening for diabetes, hypertension etc); for this reason, a shared-care model between the oncologist and the general practitioner delivers the most comprehensive care to promote wellness among cancer survivors
Knowledge	• Familiarity with the risks of long-term and late effects of different cancer treatments and the interaction with comorbidities, medications, lifestyle, age and family risk • Familiarity with the indications for and the limitations of the different diagnostic imaging modalities for screening for cancer recurrence and second cancers, as well as their psychological and financial impact • Understanding of the importance of offering individualised treatment based on age, comorbidities, lifestyle, family history and cancer recurrence risk • Understanding of the importance of educating patients, family, caregivers and primary care providers about the risks of cancer recurrence, familial/genetic risks, long-term and late side effects and maintaining healthy lifestyles

9. SURVIVORSHIP	
by Elizabeth Charlotte Moser, Charles L Shapiro and Lifang Liu	
Ability	• Ability to contribute actively to multidisciplinary discussions and patient presentations taking into account age, sex, cancer recurrence risk, lifestyle, comorbidities and consequences of cancer treatments • Ability to discuss critically the treatment options/recommendations of screening for cancer recurrences and second cancers, long-term and late effects, promoting empowerment and wellness among survivors and their families/caregivers by teaching or referring them to programmes/primary care providers that emphasise the importance of adopting healthier lifestyles and the importance of obtaining routine preventative healthcare • Ability to perform a thorough history, physical examination, laboratory studies and diagnostic imaging as indicated for new or persistent symptoms in cancer survivors • Ability to discuss secondary prevention strategies with patients, family and related specialists • Ability to discuss potential social challenges patients may face, such as job interruption during treatment

Thank you for your attention See you at ESMO Madrid this september

photo taken in Chicago during ASCO 2015