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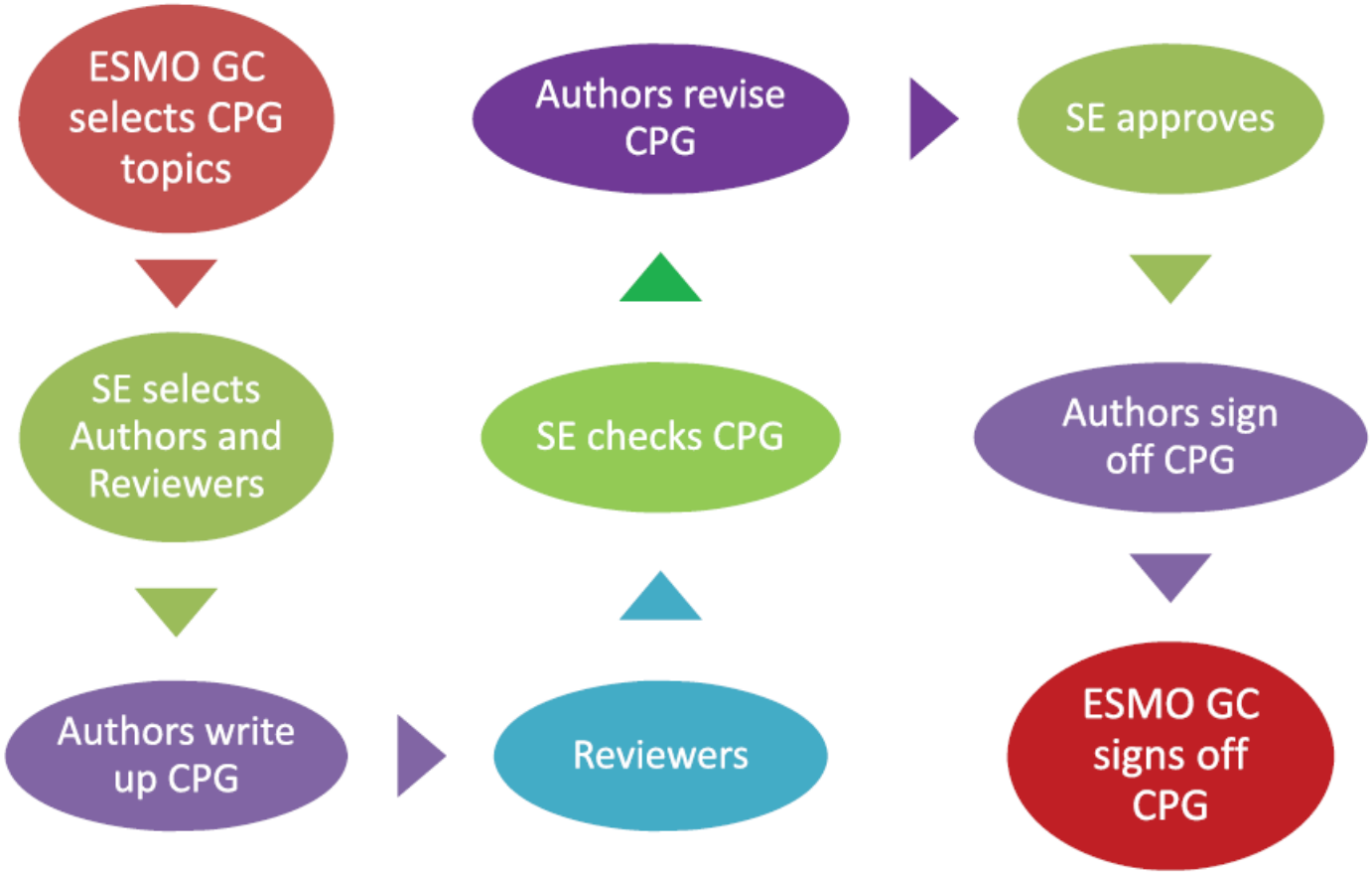
BEST PRACTICE

ESMO GUIDELINES

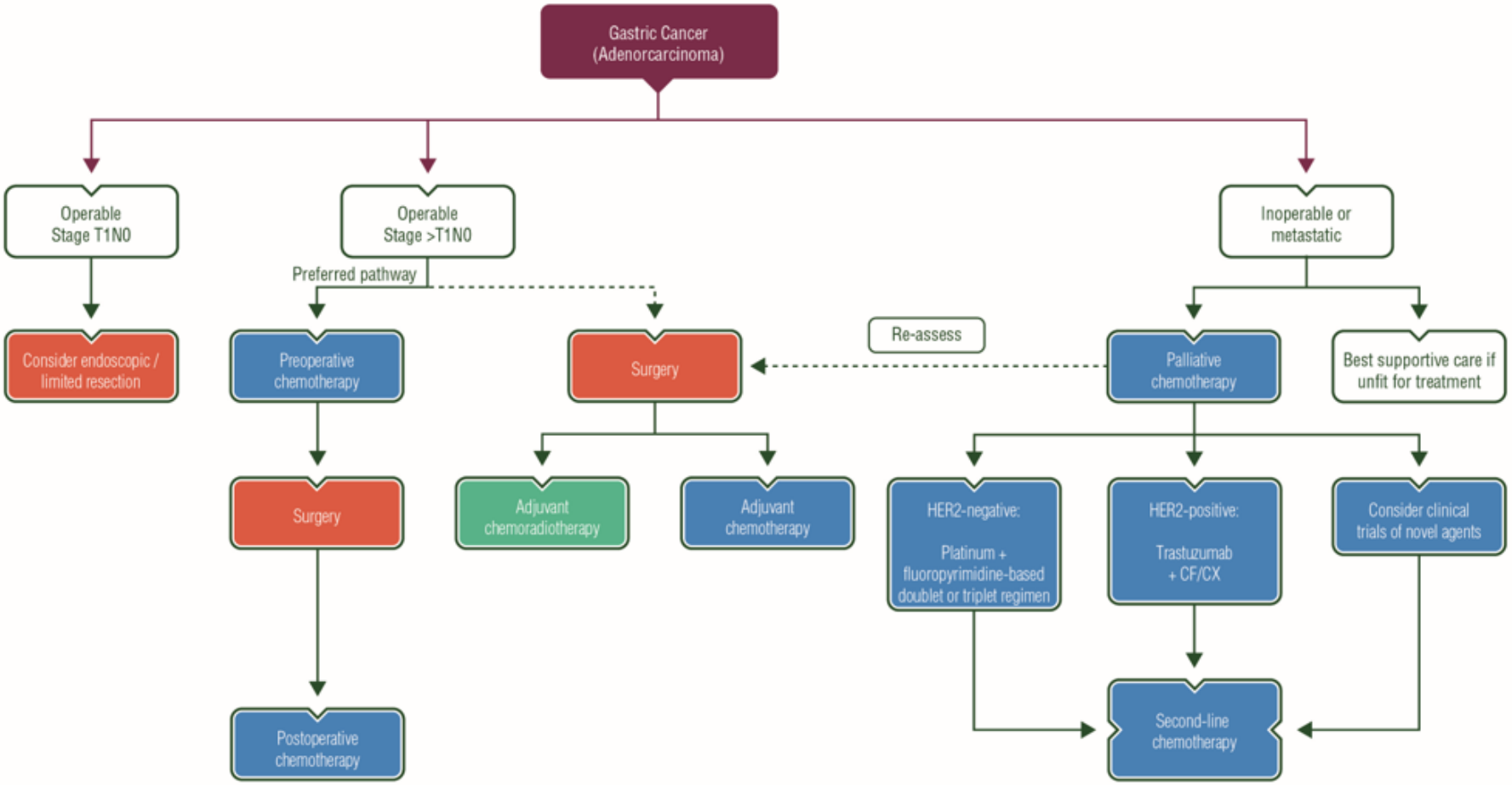
Report

George Pentheroudakis

ESMO CPG PRODUCTION PROCESS



New standardised features

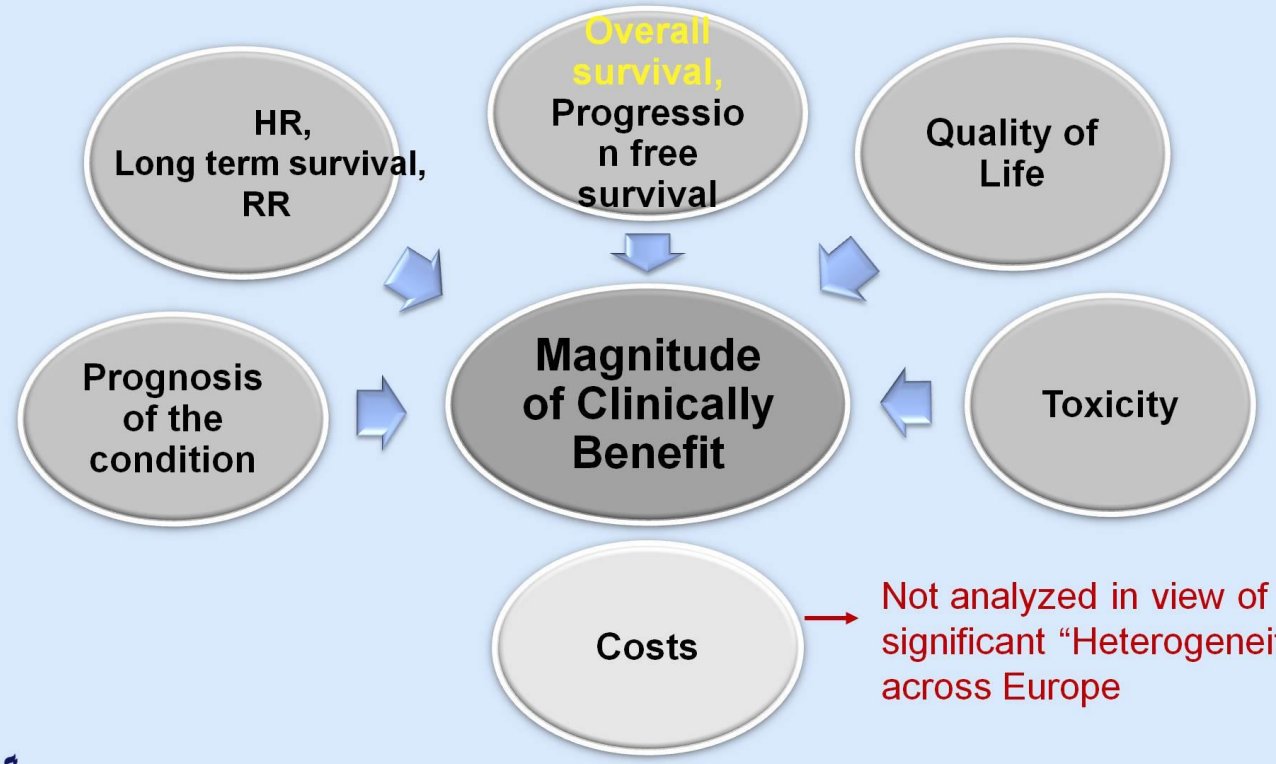


New standardised features

Personalised medicine synopsis table for metastatic NSCLC

Biomarker	Method	Use	LOE, GOR
EGFR mutation	Any appropriate validated method, subject to external quality assurance.	Used to select patients for EGFR TKI therapy, identifying those, with sensitizing mutations, most likely to respond	V, A
ALK gene rearrangement	Any appropriate validated method, subject to external quality assurance. Standard approach has been FISH, or less often, multiplex PCR or RT-PCR. Certain IHC approaches may be used as a substitute primary test. IHC may also be used to screen patients, positive cases confirmed by an orthogonal method (FISH, PCR)	Used to select patients for ALK tyrosine kinase inhibitor therapy, identifying those, with a positive test, most likely to respond	V, A

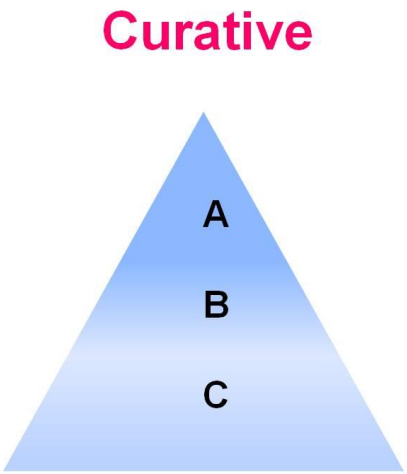
Factors taken into account for ESMO-MCBS

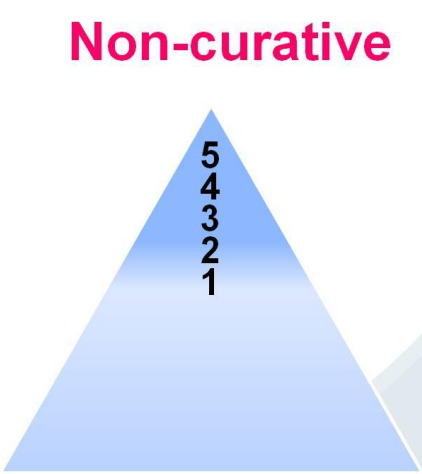


Presented By Lowell Schnipper at 2016 ASCO Annual Meeting

ESMO-MCBS substantial improvements

- Curative setting A & B or non-curative setting 5 & 4





Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

ASCO

NON CURATIVE OS

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ESMO Magnitude of Clinical Benefit Scale

Form 2a: for therapies that are not likely to be curative with primary endpoint of OS

Name of study:			
Study drug:	Indication:		
First author:	Year:	Journal:	
Name of evaluator:			

IF median OS with the standard treatment is ≤ 1 year

Grade 4	Mark with X if relevant
HR ≤ 0.65 AND Gain ≥ 3 months	
Increase in 2 year survival alone ≥ 10%	

Grade 3	
HR ≤ 0.65 AND Gain 2.5-2.9 months	
Increase in 2 year survival alone 5 - <10%	

Grade 2	
HR > 0.65-0.70 AND Gain 1.5-2.4 months	
Increase in 2 year survival alone 3 - <5%	

Grade 1	
HR > 0.70 OR Gain <1.5 months	
Increase in 2 year survival alone <3%	

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IF median OS with the standard treatment is ≤ 1 year

Preliminary magnitude of clinical benefit grade (highest grade scored)

4	3	2	1

Quality of Life assessment/grade 3-4 toxicities assessment *

Does secondary endpoint quality of life show improvement	
Are there statistically significantly less grade 3-4 toxicities impacting on daily well-being*	

*This does not include alopecia, myelosuppression, but rather chronic nausea, diarrhoea, fatigue, etc.

Adjustments

Upgrade 1 level if improved quality of life and/or less grade 3-4 toxicities impacting daily well-being are shown

Final adjusted magnitude of clinical benefit grade

5	4	3	2	1

IF median OS with the standard treatment > 1 year

Grade 4	Mark with X if relevant
HR ≤ 0.70 AND Gain ≥ 5 months	
Increase in 3 year survival alone ≥ 10%	

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Grade 3	
HR ≤ 0.70 AND Gain 3-4.9 months	
Increase in 3 year survival alone 5 - <10%	

Grade 2	
HR > 0.70-0.75 AND Gain 1.5-2.9 months	
Increase in 3 year survival alone 3 - <5%	

Grade 1	
HR > 0.75 OR Gain <1.5 months	
Increase in 3 year survival alone <3%	

Preliminary magnitude of clinical benefit grade (highest grade scored)

4	3	2	1

Quality of Life assessment /grade 3-4 toxicities assessment*

Does secondary endpoint quality of life show improvement	
Are there statistically significantly less grade 3-4 toxicities impacting on daily well-being*	

*This does not include alopecia, myelosuppression, but rather chronic nausea, diarrhoea, fatigue, etc.

Adjustments

Upgrade 1 level if improved quality of life and/or less grade 3-4 toxicities impacting daily well-being are shown

Final adjusted magnitude of clinical benefit grade

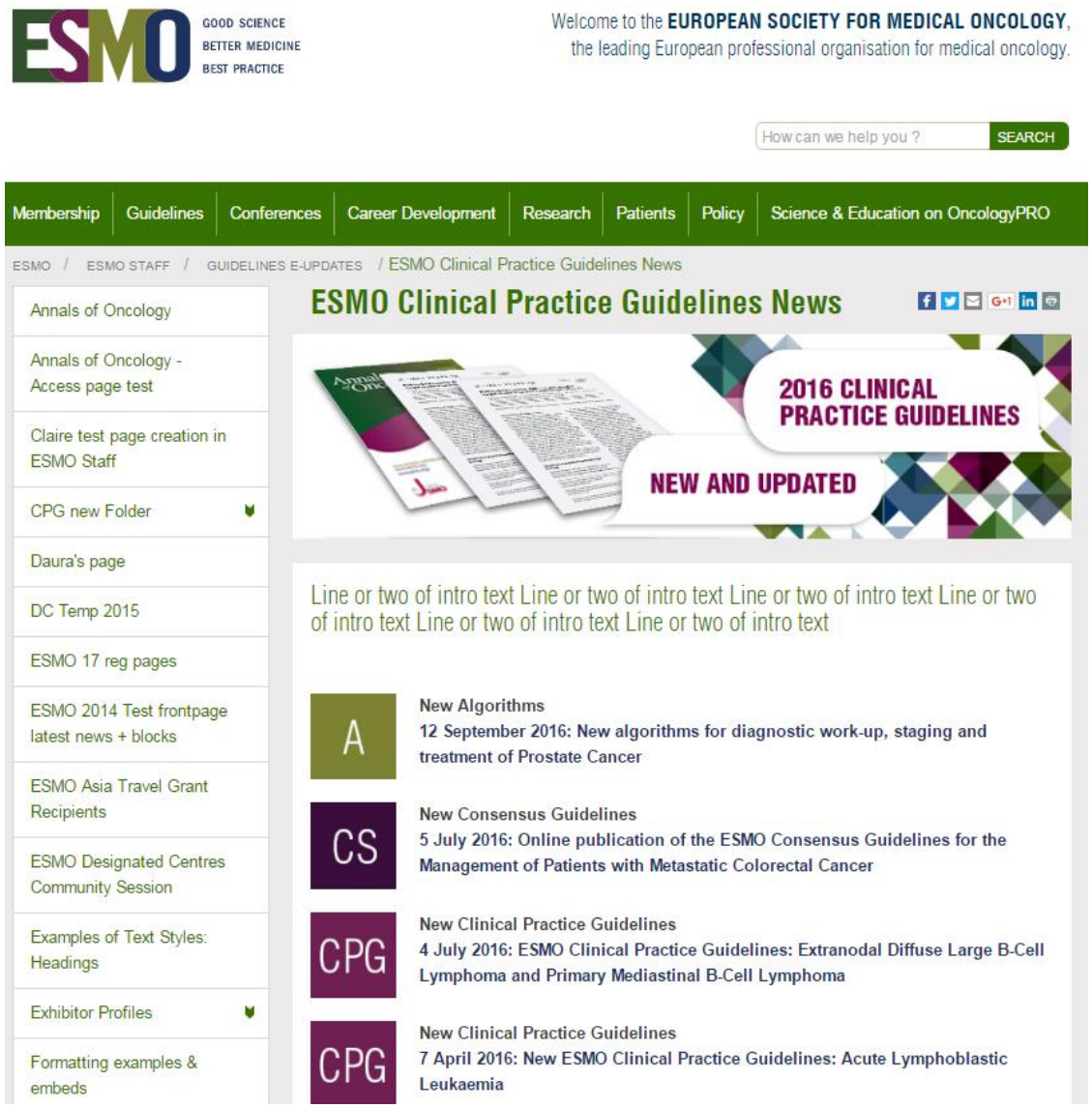
5	4	3	2	1

ESMO-MCBS – inclusion of scores in Guidelines

Metastatic NSCLC (continued)

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/ toxicity	MCBS score[b]
Nivolumab	Advanced	Nivolumab versus docetaxel in advanced squamous-cell NSCLC [98] Phase III NCT01642004	Docetaxel in patients with advanced SCC who have disease progression during or after 1st-line chemotherapy. Control OS 6 months	OS gain: 3.2 months. 2-year survival gain 15%	OS: HR for death 0.59 (0.44-0.79)	Improved toxicity profile	**5** (Form 2a)[c]
Nivolumab	Advanced	Nivolumab versus docetaxel in advanced non-squamous NSCLC [104] Phase III NCT01673867	Docetaxel in patients with NSCC who progressed during or after platinum-based doublet chemotherapy. Control OS 9.4 months	OS gain: 2.8 months. 2-year survival gain 16%	OS: HR for death 0.73 (0.59-0.89)	Improved toxicity profile	**5** (Form 2a)
Pembrolizumab	Advanced	Pembrolizumab vs docetaxel for previously treated, PD-L1-positive, advanced NSCLC (KEYNOTE-010): a randomised controlled trial [96] Phase III NCT01905657	Docetaxel in patients with previously treated, PD-L1-positive, advanced NSCLC. Control OS 8.5 months	In PD-L1 >1%:[d] OS gain: 1.9 months In PD- L1 >50%:[d] OS gain: 6.7 months	In PD-L1 >1%:[d] OS: HR for death 0.71 (0.58–0.88) In PD-L1 >50%:[d] OS: HR for death 0.54 (0.38–0.77)	Improved toxicity profile	**In PD-L1 >1%: 3** (Form 2a) **In PD-L1 >50%: 5** (Form 2a)

ESMO Guidelines: news page on esmo.org



ESMO Guidelines eUpdates: example

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Welcome to the **EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY**, the leading European professional organisation for medical oncology.

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Membership | Guidelines | Conferences | Career Development | Research | Patients | Policy | Science & Education on OncologyPRO

ESMO / ESMO STAFF / GUIDELINES E-UPDATES / eUpdate - Cutaneous melanoma

eUpdate - Cutaneous melanoma: ESMO Clinical Practice Guidelines

eUpdate - Cutaneous melanoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

Dummer R, Hauschild A, Lindenblatt N, et al. Ann Oncol (2015) 26 (suppl 5): v126-v132.

» Section and Text

In a double-blinded prospective randomised trial, nivolumab was compared with ipilimumab and the ipilimumab/nivolumab combination. Nivolumab monotherapy compared to ipilimumab was scored with an ESMO Magnitude of Clinical Benefit Scale (MCBS) score of 4, as it resulted in a statistically and clinically significant progression-free survival (PFS) benefit, without increased toxicity. The nivolumab+ipilimumab combination was scored with an ESMO-MCBS score of 2, the lower score reflecting the presence of only PFS data as well as the increased toxicity of the combination. Programmed death ligand 1 (PD-L1) expression may be a relevant marker in this context, however data are not available nor mature for the ESMO-MCBS scoring of the nivolumab+ipilimumab combination compared to ipilimumab in the PD-L1-negative melanoma subgroup of patients.

» Recommendation

For patients with metastatic melanoma, treatment options for first-line setting include the anti-PD-1 antibody nivolumab which showed a clinically and statistically significant PFS benefit over ipilimumab, with a high MCBS score of 4 [II, B].

» Reference

Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. N Engl J Med 2015;373:23-34.

» Magnitude of Clinical Benefit Scale (MCBS) table for new therapies/indications in Cutaneous Melanoma*

Therapy	Disease setting	Trial	Control	Absolute survival	HR (95% CI)	QoL/toxicity	MCBS score**

eUpdate – Neuroendocrine Tumours Treatment Recommendations

eUpdate – Neuroendocrine Tumours Treatment Recommendations

Published: 20 September 2016. Authors: ESMO Guidelines Committee

Clinical Practice Guidelines

This update refers to the **Neuroendocrine bronchial and thymic tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (/Guidelines/Neuroendocrine-Tumours/Neuroendocrine-Bronchial-and-Thymic-Tumours)**, Öberg K, Hellman P, Ferolla P and Papotti A, Ann Oncol 2012; 23 (Suppl 7): vii120-vii123; and the **Neuroendocrine gastro-entero-pancreatic tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (/Guidelines/Neuroendocrine-Tumours/Neuroendocrine-Gastroenteropancreatic-Tumours)**, Öberg K, Knigge U, Kwekkeboom D and Perren A, Ann Oncol 2012; 23 (Suppl 7): vii124-vii130.

Section

Management of advanced/metastatic disease

Text update

In the randomised, double-blind, placebo-controlled, phase III RADIANT-4 trial, 302 patients with advanced, progressive, well-differentiated, non-functional neuroendocrine tumours of lung or gastrointestinal origin were randomised in a 2:1 ratio to everolimus 10 mg per day orally or placebo, both with supportive care. The primary endpoint was progression-free survival (PFS), while overall survival (OS) and quality of life were secondary endpoints. Median PFS was 11.0 months (95% CI 9.2–13.3) in the everolimus group and 3·9 months (3.6–7.4) in the placebo group (hazard ratio [HR] 0.48 [95% CI 0.35–0.67], p<0·00001). Although not statistically significant, the results of the first pre-planned interim OS analysis indicated that everolimus might be associated with a reduction in the risk of death (HR 0.64 [95% CI 0.40–1.05], one-sided p=0.037). Grade 3 or 4 drug-related adverse events were infrequent and manageable, though more numerous in the everolimus group.

Recommendation

In patients with unresectable or metastatic, well-differentiated (Grade 1 or Grade 2) non-functional neuroendocrine tumours of gastrointestinal or lung origin with progressive disease, everolimus, as compared with placebo, is associated with a statistically and clinically significant improvement in PFS.In the absence of mature OS and quality of life data, the observed PFS benefit is associated with an ESMO Magnitude of Clinical Benefit Scale (MCBS) score of 3.

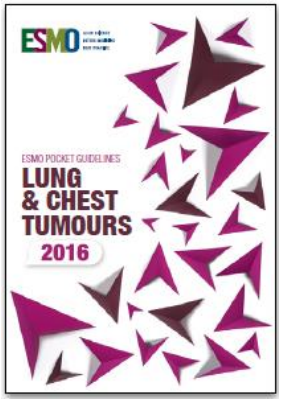
Magnitude of Clinical Benefit Scale (MCBS) table for new therapies/indications in neuroendocrine tumours (bronchial, thymic and gastro-entero-pancreatic)*

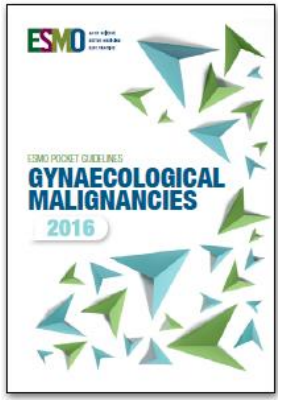
Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/toxicity	MCBS score**
Everolimus, an mTOR inhibitor	Unresectable or metastatic, well-differentiated (Grade 1 or Grade 2) non-functional neuroendocrine tumours of gastrointestinal or lung origin in adults with progressive disease	Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study [1] Phase III NCT01524783	Placebo Median PFS: 3.9 months	PFS gain: 7.1 months OS benefit, not statistically significant yet	PFS HR: 0.48 (0.35-0.67)	Deteriorated toxicity profile. QoL was a secondary endpoint, however no data are available yet.	3 (Form 2b; mature data on OS not available, data on QoL assessment not available)

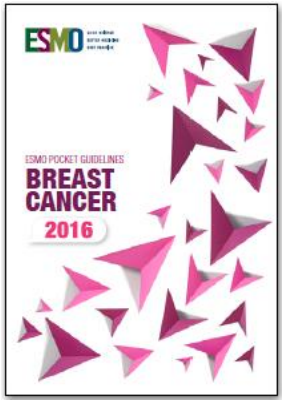
POCKET GUIDELINES 2016

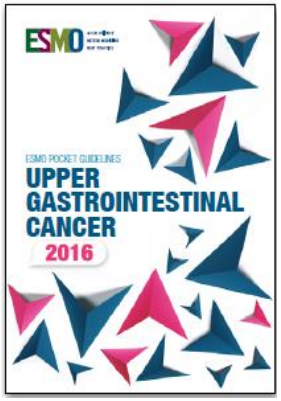
- The following titles are in preparation:

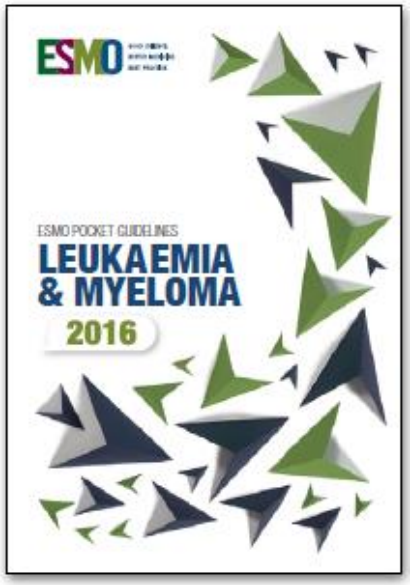
Lung & Chest Tumours
Gynaecological Malignancies
Breast cancer
Upper GI Cancer
Lower GI Cancer
Urogenital Cancer
Lymphomas
Leukaemias & Myeloma NEW
Supportive Care

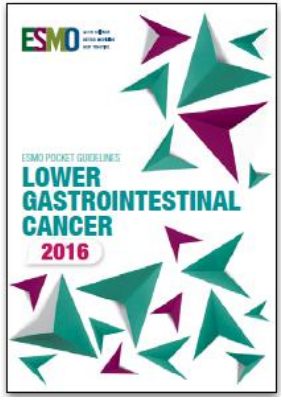


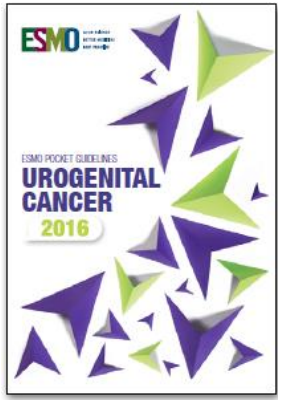


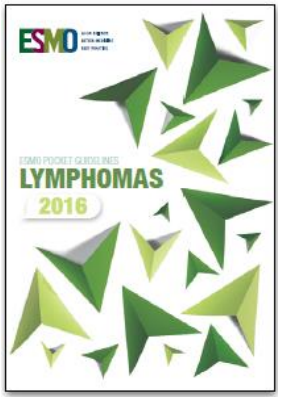


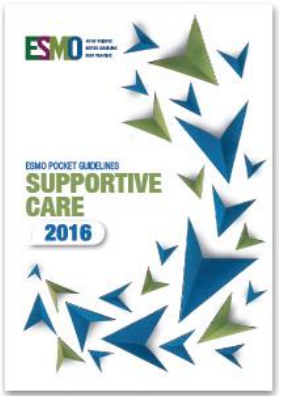










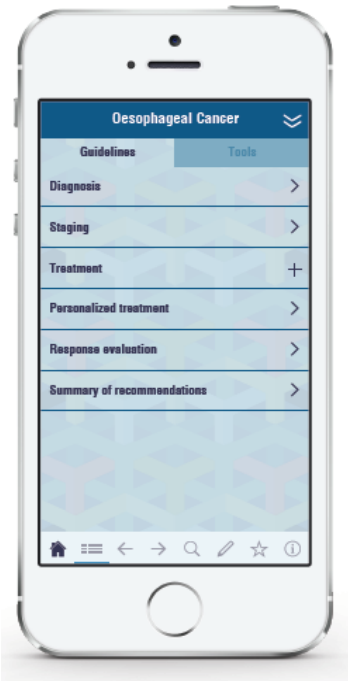


Interactive Guidelines App

Main Homescreen

Guidelines Homescreen

Guideline TOC (Closed)



- Existing sections (to be updated):
  - Lung & Chest tumours
  - Urogenital Cancers
  - Upper GI
  - Lower GI
- New sections (to be added):
  - Lymphoma
  - Supportive care