Onkološki Inštitut
Institute of Oncology
Ljubljana 80 let years

KATEDRA ZA ONKOLOGIJO
SEKCIJA ZA INTERNISTIČNO ONKOLOGIJO

Slovensko Zdravniško Društvo

#1. SUMMER SCHOOL IN MEDICAL ONCOLOGY

Part 1 – Tuesday (3.9.) & Wednesday (4.9.)

LJUBLJANA
3-6. SEPTEMBER 2019

Strokovni odbor:
izr. prof. dr. Janja Ocvirk, dr.med.
doc. dr. Martina Reberšek, dr.med.
dr. Tanja Mesti, dr.med.
Marko Boc, dr.med.

Organizacijski odbor:
izr. prof. dr. Janja Ocvirk, dr.med.
doc. dr. Martina Reberšek, dr.med.
dr. Tanja Mesti, dr.med.
Marko Boc, dr.med.
ga. Lidija Kristan

Uredniki zbornika:
Marko Boc, dr.med.
doc. dr. Martina Reberšek, dr.med.
izr. prof. dr. Janja Ocvirk, dr.med.
dr. Tanja Mesti, dr.med.

Organizator in izdajatelj (založnik):
Onkološki inštitut Ljubljana
Sekcija za internistično onkologijo
Katedra za onkologijo

Ljubljana, september 2019

AGENDA & INDEX

Tuesday, September 3

10:30-11:00	Registration of participants	
Part 1	***Moderators: dr. Dobrila, dr. Boc***	
11:00-11:30	Neoadjuvant and Adjuvant treatment strategies for gastric cancer (dr. Boc)	
11:30-12:15	Systemic treatment of metastatic gastric cancer (dr. Dobrila)	
12:15-12:35	Neoadjuvant and Adjuvant treatment strategies for pancreatic cancer (dr. Mesti)	
12:35-13:15	Systemic treatment of metastatic pancreatic cancer (dr. Mesti)	
13:15-13:30	Discussion	
13:30-14:30	Lunch break	
Part 2	***Moderators: dr. Pleština, dr. Hlebanja***	
14:30-14:50	Satellite symposium	
14:50-15:20	Systemic treatment of biliary tract cancer (dr. Reberšek)	
15:20-15:40	Systemic treatment strategies for HCC (dr. Mesti)	
15:40-16:10	Adjuvant treatment strategies for colorectal cancer (dr. Ignjatović, dr. Ocvirk)	
16:10-16:55	Systemic treatment of metastatic colorectal cancer (dr. Pleština)	
16:55-17:10	Discussion	

Wednesday, September 4

Part 1	***Moderators: dr. Radosavljevič, dr. Grašič Kuhar***	
8:30-9:15	Neoadjuvant and Adjuvant treatment strategies for lung cancer (dr. Radosavljevič)	
9:15-10:00	Systemic treatment of metastatic lung cancer (dr. Zarić)	
10:00-10:45	Systemic treatment of head and neck cancer (dr. Grašič Kuhar)	
10:45-11:00	Break	
11:00-11:30	Systemic treatment of patients with unknown primary tumor (dr. Matos)	
11:30-11:45	Systemic treatment of germinal tumors (dr. Škrbinc)	
11:45-12:15	Discussion	
12:15-12:45	Satellite symposium (Roche)	
12:45-13:45	"First line treatment of metastatic NSCLC" (*dr. Maximilian J. Hochmair*)	
13:45-14:30	Lunch break	
Part 2	***Moderators: dr. Belev, dr. Šeruga***	
14:30-15:15	Systemic treatment of prostate cancer (dr. Belev)	
15:15-16:00	Systemic treatment of RCC (dr. Šeruga)	
16:00-16:15	Break	
16:15-16:45	The systemic treatment of the bladder cancer (dr. Mencinger)	
16:45-17:15	The palliative care - when to start and how to lead the patient and the patients family through the process (dr. Ebert Moltara)	
17:15-18:15	Interesting cases from audience	

PERI-OPERATIVE TREATMENT OF GASTRIC CANCER

Marko Boc, dr.med.
Sector of medical oncology
Institute of Oncology Ljubljana
SLOVENIA

Ljubljana, 3-6. september 2019

Summary

- Peri-operative chemotherapy (pre- and post-operative) is standard of care for unmetastatic resectable gastric cancer ≥ Stage IB **(ESMO: I,A):**
  - Peri-operative chemotherapy comprises a platinum compaund and a fluoropyrimidine,
  - Addition of epirubicine is optional (toxicity), strongest evidence for cisplatin/fluorouracil ± epirubicine,
- Taxanes improve peri-operative chemoterapy response and improve survival outcomes trough better response.
- For patients ≥ Stage IB gastric cancer who have undergone surgery without administration of pre-operative chemotherapy or post-operative CRT, **adjuvant chemotherapy** is recommended (**ESMO: I,A):**
  - S-1 (**1,A)** and XELOX in Asian pupulation
  - 6% absolute benefit for 5-FU based chemotherapy, [HR 0.82 (0.76-0.90), p<.0001] **(ESMO: 1,A).**

Summary

- Post-operative CTX intensification did not improve outcomes!
- Since capecitabine avoids the need for an central venous access device, and is non-inferior to 5-FU in the advanced disease setting, capecitabine-containing regimens can also be suggested in the peri-operative setting **(ESMO: IV,C).**
- For patients with ≥Stage IB gastric cancer who have undergone surgery without administration of preoperative chemotherapy, **postoperative chemoradiotherapy (CRT) (ESMO: I,A).**
- For patients having undergone preoperative chemotherapy, the addition of postoperative radiotherapy (RT) has no added benefit.

PANCREATIC ADENOCARCINOMA

TANJA MESTI, MD, PHD

INSTITUTE OF ONCOLOGY LJUBLJANA

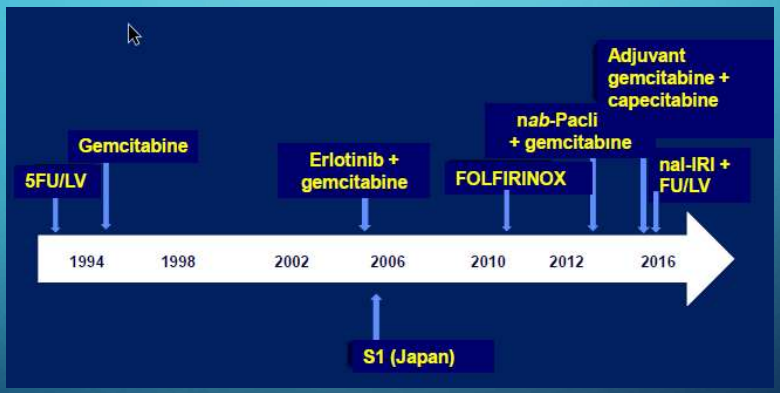
ADJUVANT TREATMENT

- Adjuvant ChT > DFS & OS
- Adjuvant ChT > operation alone
- m- FOLFIRINOX the best, but the most toxic option
- m- FOLFIRINOX - PS (0-1)

NEOADJUVANT TREATMENT

- Limited data
- Best recommended (m)FOLFIRINOX ± RT or
  gemcitabin + nab-paklitaksel ± RT
- Tertiary care centers
- **Multidisciplinary planning**

SYSTEMIC TREATMENT FOR METASTATIC DISEASE



Van Custeem E. ESMO Academy 2017

CONCLUSIONS

- Initially CT th/abd
- CA 19-9
- **Multidisciplinary approach**
- Treatment according to the guidelines
- Pts preferences, tumour burden, comorbidities

CONCLUSIONS

- Inclusion in the clinical studies if possible
- Systemic treatment for advanced or metastatic pancreatic adenocarcinoma < symptoms and tumour burden and > survival
- **GOOD PALLIATIVE CARE – EARLY**

Systemic treatment of biliary tract cancers

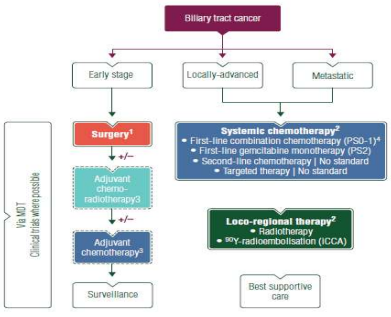
1st Summer school in medical oncology - standards and open questions

ASSIST.PROF.MARTINA REBERŠEK, MD

DEPARTMENT OF MEDICAL ONCOLOGY

INSTITUTE OF ONCOLOGY LJUBLJANA

J. W. Valle, et al. On behalf of the ESMO Guidelines Committee Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up- 2016



[1] Special considerations:
- Need for pre-operative biliary drainage
- Avoid percutaneous biopsy in resectable disease
- Assess Future Liver Remnant
- Assess need for Portal Vein Embolisation
- Neoadjuvant approach (selected cases)
- Completion surgery for incidental gallbladder cancer of T-stage T1b and above

[2] Option of salvage surgery should be considered in responding patients with initially inoperable disease
[3] Level of recommendation IV,C
[4] Cisplatin and gemcitabine [category IA], other gemcitabine-based combination [category IIB]

Figure 1. Algorithm for the management of patients with biliary tract cancer. MDT, multidisciplinary team; PS, performance status; iCCA, intrahepatic cholangiocarcinoma.

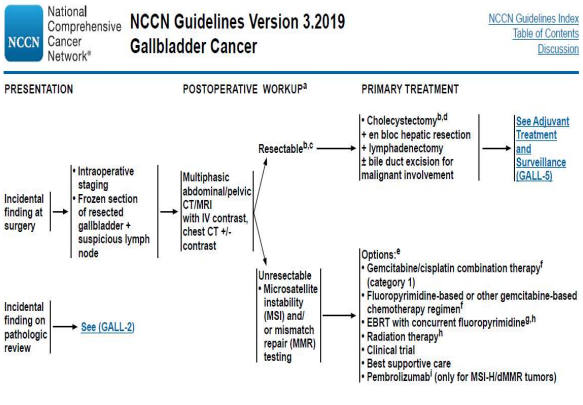
Annals of Oncology 27 (Supplement 5): v28–v37, 2016 doi:10.1093/annonc/mdw324

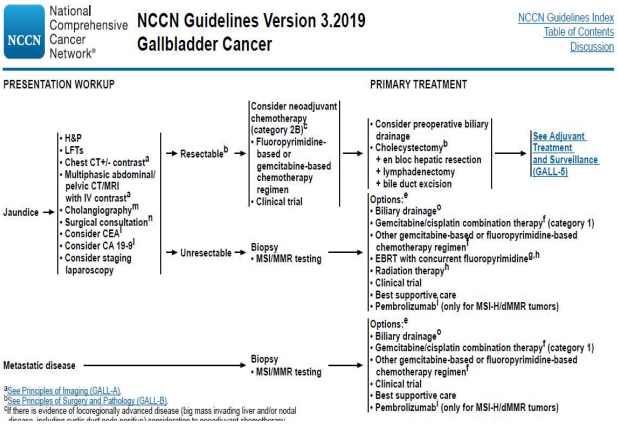
NCCN and ESMO guidelines for adjuvant systemic treatment

Cancer Type	Guideline: NCCN[40]	Guideline: ESMO[41]
Gallbladder		
R0/N0 or CIS at margin	Observation or FU CRT or FU- or gemcitabine-based CT or Clinical trial	± adjuvant chemotherapy, radiation or CRT after risk-benefit assessment
R1 or R2 or node positive	FU CRT then FU- or gemcitabine-based CT or FU- or gemcitabine-based CT ± FU CRT or Clinical trial	
Intrahepatic cholangiocarcinoma		
R0	Observation or Clinical trial or FU- or gemcitabine-based CT	± adjuvant chemotherapy, radiation, or CRT after risk-benefit assessment
R1 or node positive	Clinical trial or FU CRT or FU- or gemcitabine-based CT ± FU CRT	
R2	Clinical trial or FU- or gemcitabine-based CT ± FU CRT or Locoregional therapy or Best supportive care	
Extrahepatic cholangiocarcinoma		
R0, N0 or CIS at margin	Observation or FU CRT or FU- or gemcitabine-based CT or Clinical trial	± adjuvant chemotherapy, radiation or CRT after risk-benefit assessment
R1 or R2 or node positive	FU CRT + FU- or gemcitabine-based CRT or FU- or gemcitabine-based CRT ± FU CRT or Clinical trial	

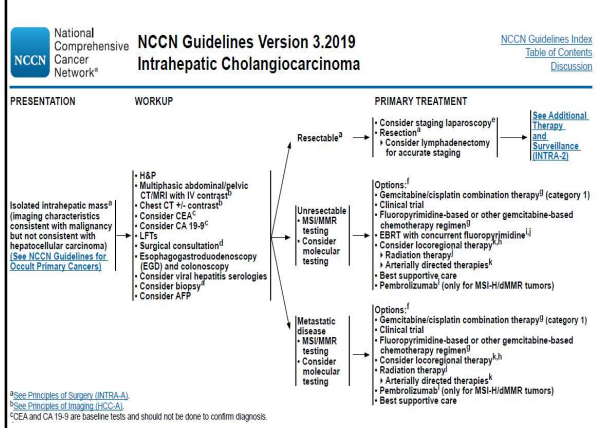
Horgan AM,Knox JJ.Adjuvant Therapy for BiliaryTract Cancers. Volume 14 / Issue 12 / December 2018 Journal of Oncology Practice, 2018; 14:12.

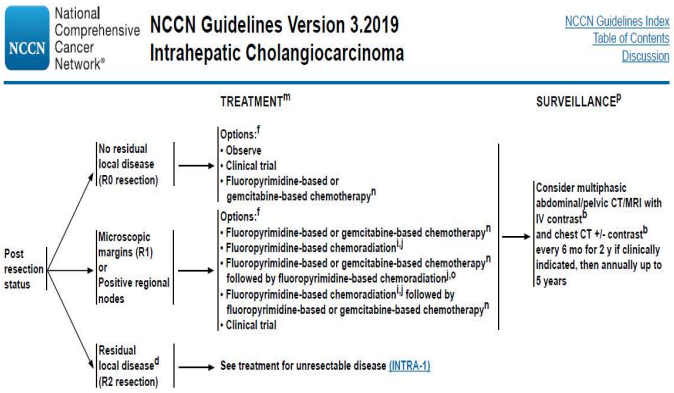
NCCN: Gallbladder cancer



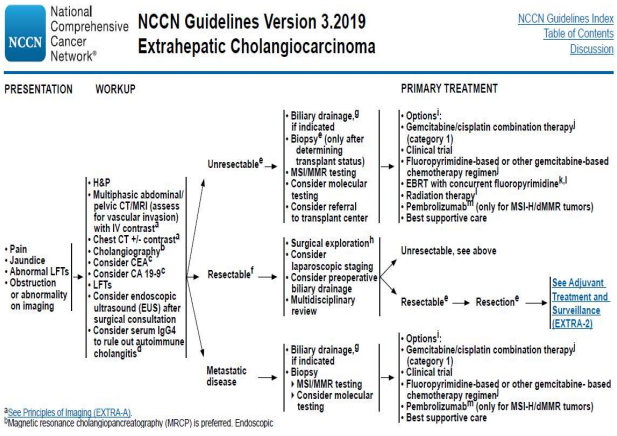


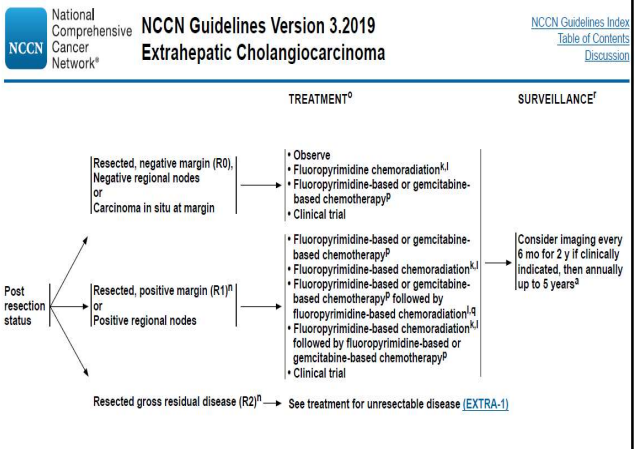
NCCN: Intrahepatic cholangiocarcinoma





NCCN: Extrahepatic cholangiocarcinoma





Conclusions(1)

- rare cancers
- poor prognosis
- important diagnostic procedures
- surgical treatment first

Conclusions (2)- systemic treatment

• **Neo- adjuvant therapy:** no standards

• **Adjuvant therapy:**

- capecitabine monotherapy

- role of radiation therapy in combination with systemic treatment- the need of prospective randomized clinical phase III trials

• **Metastatic disease:**

- 1st line: gemcitabine + cisplatin (PS ECOG 0-1), gemcitabine mono (PS ECOG 2)

- 2nd line: no standard therapy

- targeted therapy: no standards

- **Immunotherapy: MSI- H**

HCC – systemic treatment strategies

TANJA MESTI, MD, PHD

INSTITUTE OF ONCOLOGY LJUBLJANA

Key Takeaways

- Sorafenib and regorafenib are the only agents approved for advanced HCC
  - Both are multikinase inhibitors with prominent antiangiogenic effects
  - Sorafenib is approved for first-line treatment
  - Regorafenib is approved for second-line treatment after sorafenib failure or intolerance
- In a head-to-head phase III trial, lenvatinib was shown to be noninferior to sorafenib and may be considered an alternative to sorafenib, particularly in patients with intolerance
- Important to recognize the class-wide side effects of these agents (eg, hand-foot skin reaction, hypertension, diarrhea, weight loss) and employ timely interventions to optimize treatment outcomes

i3Health

Landscape-Second line therapy for HCC

		Total N	PFS benefit	OS benefit	RR
CHECKMATE040 (SINGLE ARM)	Nivolumab*	154	NA	NA median OS ≈15 mo*	14%
RESOURCE	Regorafenib* v placebo	573 (2:1)	+1.6 mo HR 0·46 (0.37-0.56); p<0·0001	+2.8 mo HR 0.63 (0.50-0.79) p<0.0001)	11%
CELESTIAL**	Cabozantinib v placebo	707 (2:1)	+3.3 mo HR=0.44 [0.36-0.52]; *P* < 0.001	+2.2 mo HR=0.76 (0.63-0.92) P = 0.0049	4%
REACH1	Ramucirumab v placebo	565	+0.7mo HR 0.63 [0.52-0.75]; p<0.0001	NO	7%
REACH 2 (AFP≥400)	**Ramucirumab v placebo**	**292 (2:1)**	**+1.2 mo HR 0.452 (0.339, 0.603) p< 0.0001**	**+1.2 mo HR 0.71 (0.531, 0.949); p=0.0199**	**4.6%**
Pooled REACH 1 / 2 (AFP≥400 subgroup)	*Ramucirumab v placebo*	*542*	*NA*	*+3.1 mo HR 0.694 (0.571, 0.842) P=0.0002*	*NA*

PRESENTED AT: 2018 ASCO ANNUAL MEETING

*FDA approved
** included 2nd and 3rd line; 2nd line update: Kelley, et al. Abstr #4088 ASCO 2018

ONKOLOŠKI INŠTITUT
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ADJUVANT TREATMENT STRATEGIES FOR COLORECTAL CANCER

1st Summer School in Medical Oncology

3. – 6. September, Ljubljana, Slovenia

Marija Ignjatović,MD

ADJ.ChT IN CRC

- ❑ **Start 4 to 8 weeks after operation**
- ❑ **Stage II**
  - ✓ **Can not be considered as a SOC for all patients**
  - ✓ **HR, pMMR: capecitabine** or 5FU **for 6 months**
  - ✓ **HR, dMMR: just <u>for very selected patients</u>, XELOX for 3 months or FOLFOX for 6 months**
- ❑ **Stage III**
  - ✓ **SOC**
  - ✓ **LR, XELOX for 3 months**
  - ✓ **HR, XELOX/FOLFOX for 6 months**

Neoadjuvant and adjuvant treatment strategies for lung cancer

Davorin Radosavljevic

Institute for Oncology and Radiology of Serbia

Belgrade

„1st Summer School in Medical Oncology - Standards and Open Question“,

September 3-6th 2019, Ljubljana, Institute of Oncology

conclusions

- adjuvant chemotherapy is established for stage II and III resected NSCLC with sustained benefit
- the regimen with most evidence is cisplatin vinorelbine although the accepted schedule differs from JBR.10 and ANITA trials
- stage IB tumours can be considered for adjuvant chemotherapy if >/= 4cm although evidence is from unplanned, retrospective analyses (CALGB 9633 and JBR.10)
- selected older patients (70+) tolerate chemotherapy with acceptable toxicity but limited evidence for elderly and very elderly (75+, 80+)
- further major improvements with chemotherapy alone are unlikely (pemetrexed?)
- research will be focused on better discrimination of high versus low risk patients, predictive factors and more targeted therapies

Conclusions

- The local/regionally advanced setting is rapidly evolving with the addition of immunotherapy
- The new standard of care in patients with unresectable disease: concurrent chemoradiation, followed by one year of durvalumab
- Future studies, exploring the role of replacing chemotherapy with immunotherapy in unresectable disease and adding adjuvant or neoadjuvant immunotherapy in resectable disease, may further reshape our standard practice

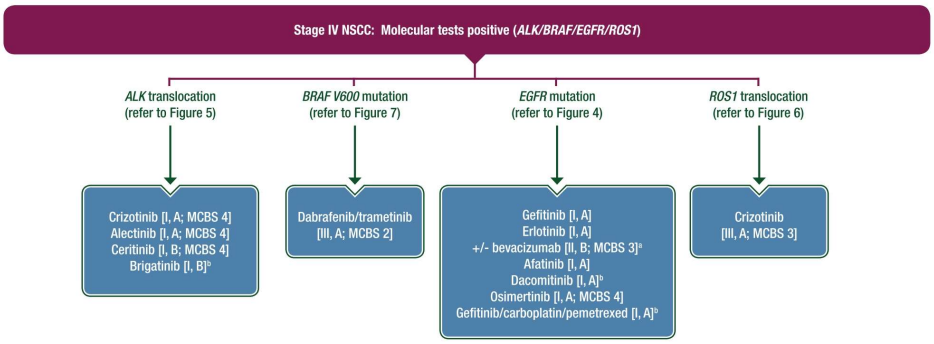
Institute for Pulmonary Diseases of Vojvodina
Faculty of Medicine, University of Novi Sad
Serbia

Systemic treatment of metastatic lung cancer

Assist. Prof dr Bojan Zarić, MD, PhD
Head, Department for diagnostics and treatment of lung cancer
Head, Clinical Trials Unit

bojan.zaric@institut.rs

Oncogene driven lung cancer treatment in first line



Oncogene driven lung cancer treatment beyond first line

- Based on molecular profiling and determination of resistance mechanism,
- Should be tailored to target secondary mutation (if any), otherwise RCT or standard platinum based doublet,
- Adequate sequencing remains to be determined.

Treatment of metastatic lung cancer without driver mutations in first line

- TPS ≥ 50% (≥1%) - pembrolizumab monotherapy,
- High TMB – Nivolumab/Ipilimumab,
- Any expression of PD-L1 – IO/Chemo combo, standard platinum based therapy.

Treatment of metastatic lung cancer without driver mutations beyond first line

- Immunotherapy if not given in first line (regardless of PD-L1 expression,
- RCT,
- Docetaxel mono or any other available (platinum) based chemotherapy.

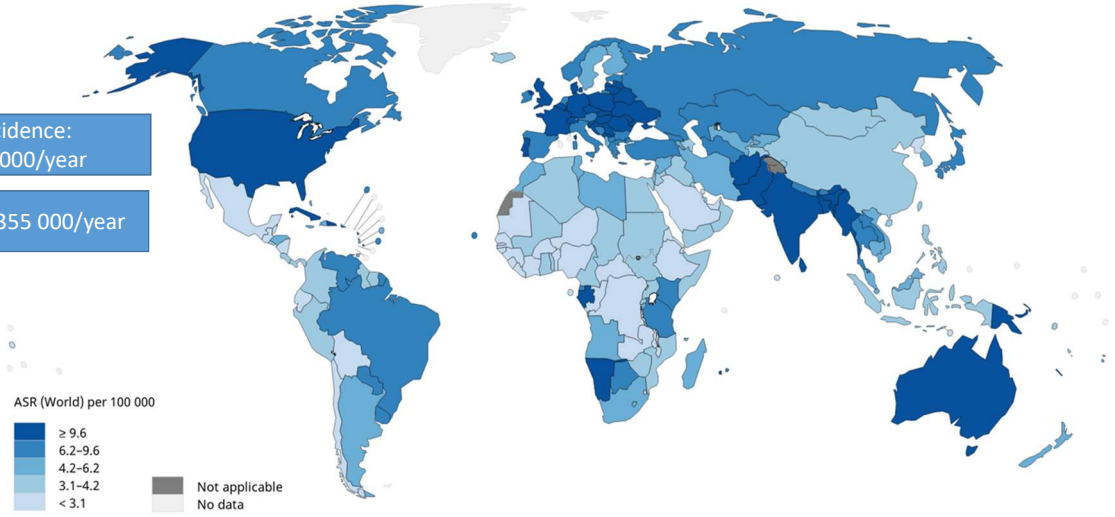
Systemic treatment of head and neck tumors

Assist. Prof. Cvetka Grašič Kuhar, MD, PhD
Institute of Oncology Ljubljana, Department of Medical Oncology

lip, oral cavity, oropharynx, larynx, hypopharynx

Accessed 15.8.2019

Estimated age-standardized incidence rates (World) in 2018, both sexes, all ages



Incidence: 640 000/year

Deaths: 355 000/year

Data source: GLOBOCAN 2018
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

Etiology, risk factors

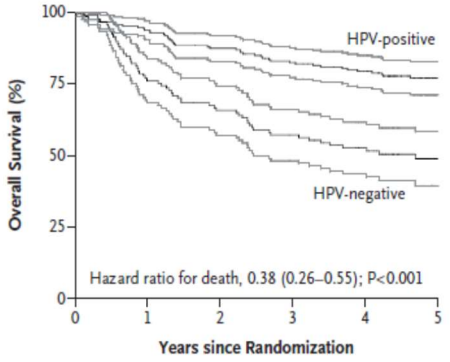
- Tobacco
- Alcohol
- HPV
- EBV
- Chewing of betel leafs
- UV-exposure (lips)
- Poor oral/dental hygiene/mechanical irritation
- Occupational hazards: wood dust, leather industry, nickel, azbestos
- Gastroesophageal reflux disease
- Genetic syndrome (i.e. Fanconi anemia)

HPV+ vs. HPV- oropharyngeal carcinoma

	HPV+	HPV-
Localisation	Tonsil, Base of toungue	All localizations
Histology	nonkeratinizing, basaloid, high grade	keratinising
Age Soc econ status Performance status	53–57 years Good Better	57–64 years, Lower Lower
Gender	3:1 for men	3:1 for men
T stage N stage	Low T (Tx, T1-2) high N stage, cystic cervical nodes	High T stage High N stage, noncystic
Molecular char. PD-L1 overexpression DNA metilation	PI3KCA mutated 49-70% more	p53 mutated 29-34% less
Risk factors	Sexual behaviour, associated with HIV in anogenital HPV, less tobacco	Tobacco, alcohol
3-year risk for metastases	9-11 %	14-15 %
3- and 8-year OS of stage III, IV	82 and 71 %	57 and 30 %

HPV is a prognostic factor

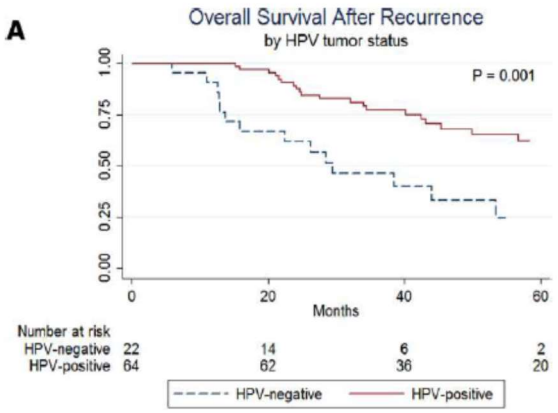
Primary



No. at Risk						
HPV-positive	206	193	179	165	151	73
HPV-negative	117	89	76	65	51	22

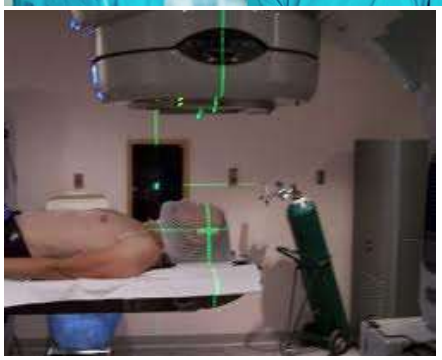
Ang et al. (2010). *New England Journal of Medicine, 363*(1), 24–35.

Recurrence



Joseph et al. Head & Neck 2016: 28 (suppl 1), E1501-9..

Treatment of early stage (stage I, II)



-one modality only
-depend on tumor localisation, patient preferences

Surgery

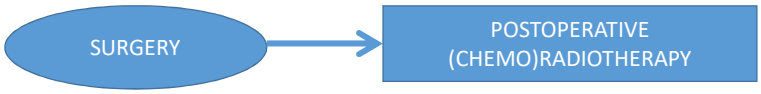
or

Radiotherapy

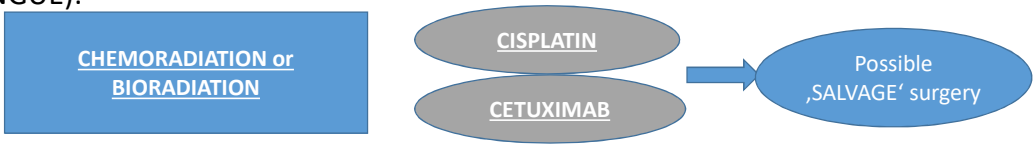
http://media-cache-ec0.pinimg.com/originals/b0/b1/11/b0b11177ebfa9dc7ae99bcce8df9bc0c.jpg

Therapy of stage III, IVa,b

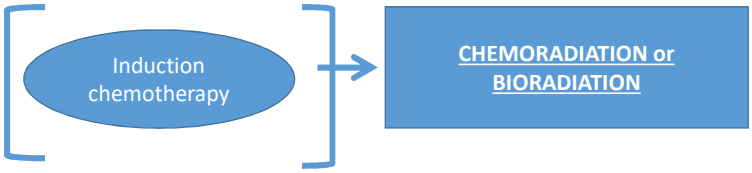
- Operable disease:



- Operable disease, but intention for organ preservation (LARINX, PHARYNX, BASE OF TOUNGUE):



- Inoperable disease:



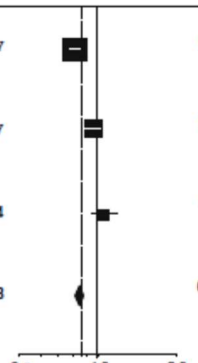
Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients

Jean-Pierre Pignon [a,*], Aurélie le Maître [a], Emilie Maillard [a], Jean Bourhis [b], on behalf of the MACH-NC Collaborative Group [1]

Radiotherapy and Oncology 92 (2009) 4–14

(a) Hazard ratio of death.

Timing	No. Deaths / No. Entered LRT+CT	LRT	O-E	Variance	Hazard Ratio	HR [95% CI]
Concomitant	3171/4824	3389/4791	-326.4	1587.7		0.81 [0.78;0.86]
Induction	1877/2740	1813/2571	-40.0	900.7		0.96 [0.90;1.02]
Adjuvant	**631/1244**	**661/1323**	**17.9**	**317.4**		**1.06 [0.95;1.18]**
Total	**5679/8808**	**5863/8685**	**-348.5**	**2805.8**		**0.88 [0.85;0.92]**



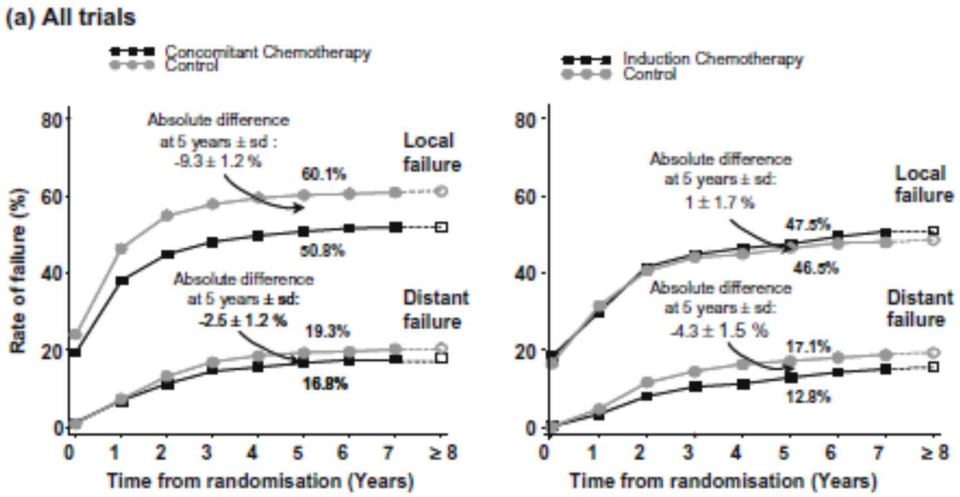
Test for heterogeneity: $\chi^2_{107} = 179.8$ $p < 0.0001$ $I^2 = 41\%$

Test for interaction: $\chi^2_2 = 26.60$ $p < 0.0001$

LRT+CT effect: p < 0.0001

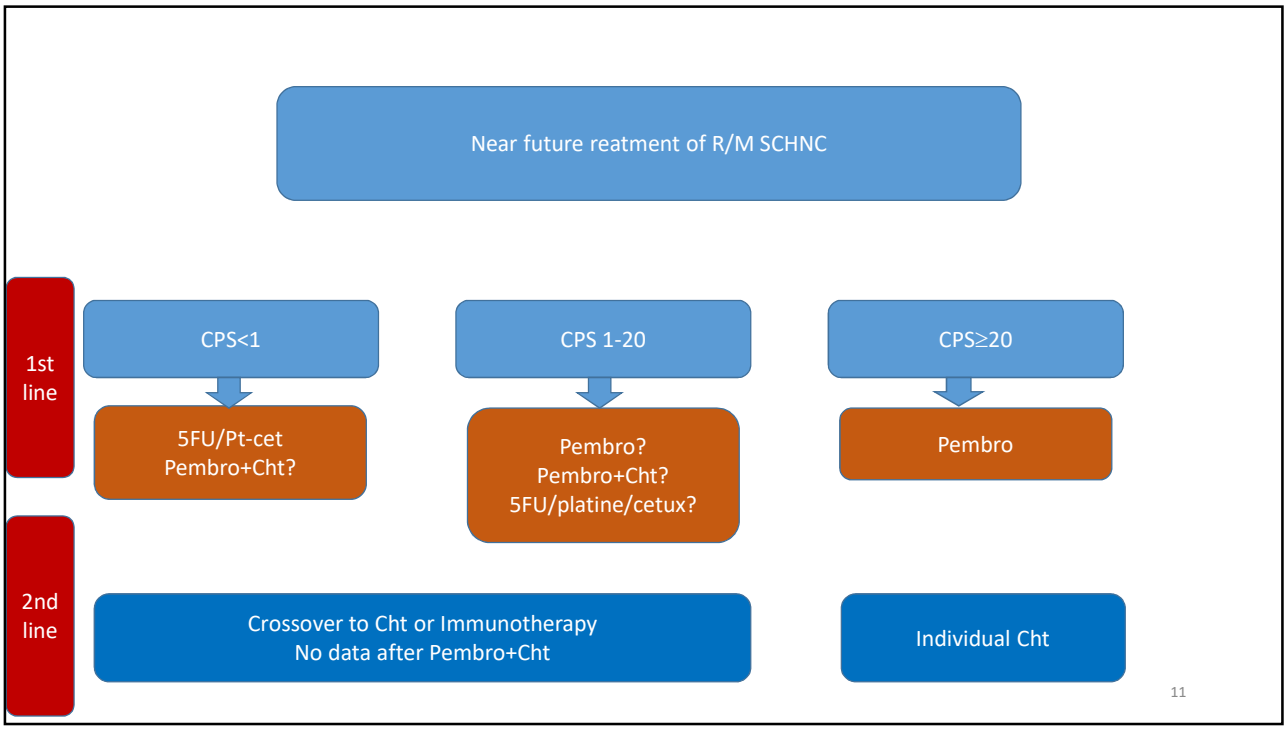
16485 pts
87 trials

Concomitant CTRT has an effect on LOCAL FAILURE and DISTANT FAILURE



Treatment of R/M SCHNC

1st line	Relapse<6 months after platine CRT → nivolumab	Reccurence>6 months after platine → 5FU/platine/cetux	Unfit for platine Cht → Individual Cht/best supportive care
2nd line	Individual Cht	Nivolumab or pembrolizumab	Nivolumab or pembrolizumab



Treatment of nasopharyngeal carcinoma: very chemo- and radiosensitive tumor

Surgery is not the option!

- Stage I: RT only
- Stage II, III, IVA:
  - Concurrent CT/RT > ACT (category 2) (ACT: 5FU/cis)
  - CT/RT (category 2a)
  - ICT > CT/RT (category 2b) (ICT: TPF, gem/cis??)
  - multimodality clinical trial

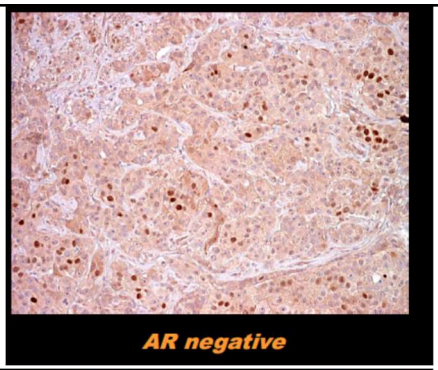
Primary metastatic or recurrent salivary carcinoma (local/regional/distant metastases)

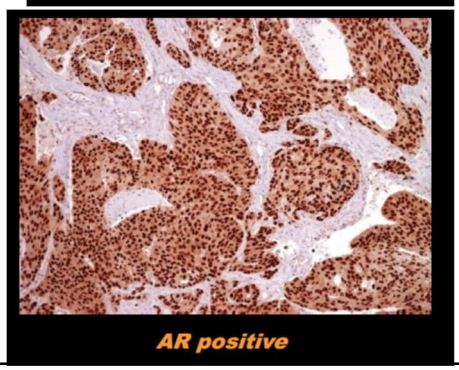
- Trial
- CT/RT
- CT > CT/RT or RT or Observation
- RT/surgery in selected pts with oligometastatic disease

- Salvage curative surgery (neck, local)
- Salvage RT (carbon or proton IMRT)
- CT (gem/cis better than 5FU/cis)
  - Other active drugs: Taxanes, IFO, FU, capecitabine, vinorelbine, gemcitabine, MTX, EDX, cetuximab (11%)
- Non active drugs: TKI
- Immunotherapy: CTL, to disrupt EBV cell latency (azacitidine..), Nivo: 20% RR, PFS at 1yr 19%

Androgen receptors in salivary gland ca. - antiandrogen therapy

- Advanced disease
- •AR high expressing cases, independently from histology (mostly SDC; AD, NOS; HG-MEC)
- •Female?
- •Which type of HT?
  - ➢ bicalutamide 50 mg/die plus LHRH agonist q4wks?
  - ➢ bicalutamide 150 mg?
- How long?





CANCER OF UNKNOWN PRIMARY SITE (CUP)

4th September 2019

Erika MATOS

Definition

- CUP is biopsy-proven malignancy for which the anatomic origin at the time of presentation remains unidentified in spite of a detailed history, physical examination and a thorough diagnostic work-up.
- CUP is a heterogeneous group of metastatic tumors, which share some common features:
  - the ability of an early dissemination,
  - clinical absence of the primary site,
  - aggressive behaviour,
  - unpredictable metastatic pattern,
  - poor response to conventional systemic cytotoxic therapy.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Incidence of CUP (1)

- Rare disease?
- CUP accounts for 3-5% of all human cancers.
- CUP is considered the 8th most frequent malignant tumor.
- During the last two decades we have evidence that the incidence is decreasing (EU and USA).
- Why is it decreasing?
  - Improved diagnostics.
    - better immunohistochemistry,
    - better imaging technology and
    - molecular analyses (gene expression profiling tests and comprehensive genomic profiling)
      - which may enable us to detect the primary site more often.
  - Better smoking control.
    - Although the etiology and risk factors for CUP are poorly defined.
    - Smoking is one of the risk factors: RR 3.6 for current smokers, RR 5.1 for a heavy smokers.

Cancer medicine 2018; 7:4814-24.
Cancer Causes Control 2014; 25:747-57.

Basic diagnostic-work-up in CUP (ESMO guidelines)

- Patient's history
  - history of previous biopsies, spontaneously regressing lesions and family history
- Physical examination
  - Including rectal and breast examination.
- Good quality tissue sample (ESENTIAL!):
  - meticulous immunohistochemistry.
- Basic blood and biochemical analyses.
- CT of the chest, abdomen and pelvis.
- Mammography in women.

Diagnostic strategy should take in account the natural behaviour of the disease and the expected duration of survival based on extent of the disease and PS.
Difficult and time-consuming diagnostic studies should not compromise patients' quality of life.

Ann Oncol 2015; 26(Suppl 5): v133-138.

Additional diagnostic-work-up in CUP (1)

- Additional procedures should be sign-, symptom-, lab. abnormalities guided.
- Breast MRI: in patients with isolated axillary lymph node metastases and suspected occult primary breast carcinoma after negative mammography and sonography results.
- Broader use of MRI in CUP diagnostics is questionable.
- Endoscopy: if the patient has symptoms or relevant signs.
- FDG-PET imaging in CUP diagnostics:
  - in patients with cervical lymphadenopathy of primarily squamous histological subtype.
  - PET-CT is useful (not been prospectively studied):
    - patients presenting with solitary metastatic disease who are candidates for curative loco-regional treatment in purpose to exclude occult metastases before extensive surgery,
    - patients with known severe iodine dye allergy
    - patients with predominant bone disease who would otherwise require either multiple MRIs or bone scans to evaluate response to therapy.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Additional diagnostic-work-up in CUP (2)

- Serum tumor markers have no proven prognostic, predictive or diagnostic assistance.
- Increased values of some tumor markers may help in guiding further diagnostics:
  - Beta human chorionic gonadotropin (beta-HCG) and alpha-fetoprotein (AFP):
    - in patients with midline tumor masses with undifferentiated histology.
  - Prostate Specific Antigen (PSA):
    - in men with adenocarcinoma and predominantly bone disease.

Unfortunately, most tumor markers (CEA, CA125, CA19-9 and CA15-3) are not specific and thus are not helpful in searching for the site of primary tumor.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Clinical presentation of patients with CUP?

- There is no unique clinical picture.
- The majority of patients presents with symptoms and signs of metastatic disease.
- There are patients with only or manly liver metastases, with lymph node metastases in mediastinal or retroperitoneal region, with axillary lymph nodes, with cervical lymph nodes, with peritoneal disease, with malignant ascites, with lung disease only or pleural effusion only, bone only disease or metastases to CNS only, although more often as a part of disseminated disease.
- Clinical presentation depends on **number of metastatic lesions** and theirs' **distribution**.
- The majority of patients has metastatic disease in more than one organ, the most often in liver, lung, bone and lymph nodes.

Ann Oncol 2015; 26(Suppl 5): v133-138.

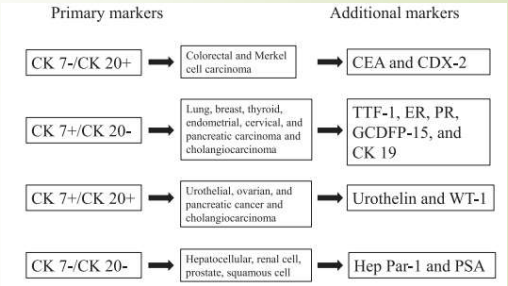
How can pathologist help? (1)

- Challenging work! Direct communication between clinician and pathologist is crucial.
- Core biopsy is preferred over fine needle aspirate specimen.
- Light microscopy: the tissue specimen (paraffin sections stained with eosine and hematoxylin)
  - Based on established cytological criteria, the pathologist usually can classify the tumors into broad groups:
    - Carcinoma (5% SSC)OR adenocarcinoma (60%),
    - Sarcoma,
    - lymphoma.
  - Some specimens will lack any cytological distinguishing features:
    - undifferentiated malignancy (35%).

Ann Oncol 2015; 26(Suppl 5): v133-138.

How can pathologist help? (2)

- IHC: significant role in the workup of CUP
  - define tumor lineage by using peroxidase-labelled antibodies against specific tumor antigens.
  - have to be directed in terms of clinical and radiological patient's data
  - random use of large numbers of tissue markers is rarely helpful
  - Staining for different CK (components of cytoskeleton of epithelial tissue) may be very helpful.
    - commonly used staining for CK7, 20, 5 and 6.
    - From the pattern of theirs' expression, the most likely site of origin can be identified. Again, the method has a limitation, no pattern is 100% specific.



The method has limitations:
- the majority of tissue markers are not specific for one organ
- no pattern is 100% specific,
- the absence of markers does not exclude the origin in certain organ/tissue.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

How can pathologist help? (3)

- Novel molecular studies in CUP evaluation?
- There are two main approaches:
  - Gene expression profiling tests (GEP) to identify the tissue of origin (ToO):
    - Methodology: RT-PCR evaluating the expression od different genes
    - Several assays on the market (evaluating from 10 to 92 and more genes)
  - Comprehensive genomic profiling tests (CGP) to find treatable genomic aberrations (GA):
    - methodology: NGS

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

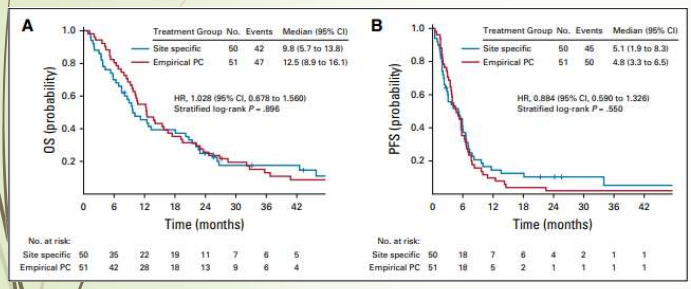
Is there a clinical benefit of identifying ToO by GEP? (1)

- GEP:
  - Has the potential to predict the origin of tumor tissue.
  - It is based on the finding that metastases have molecular signatures that may resemble to ToO.
  - The strategy has been validated in metastatic tumors with known primary site with an accuracy of 80% to 90%.

Survival of patients who received tissue-specific therapy did not differ significantly to historical cohorts, treated with empiric chemotherapy.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Is there a clinical benefit of identifying ToO by GEP? (3)



Conclusion: Site-directed therapy based on microarray profiling does not improve OS or PFS compared to empirical treatment.

Hayashi H et al. JCO 2019; 37:570-9.

- ASCO 2019:
  - prospective phase II randomized study
  - 130 patients included
  - Randomization: site-specific therapy or empiric paclitaxel and carboplatin
  - GEP was used to successfully predict a tissue of origin **in all patients**.
  - **The results were disappointing.**
    - mOS: 9,8 mos for he site-specific therapy and 12,5 mos for empiric treatment (p=0,896).
    - mPFS: 5,1 mos vs 4,8 mos (p=0,55).

Current clinical role of comprehensive gene profiling (CGP) in CUP? (1)

- The trend across all cancer types is personalized medicine (CUP seem ideal candidate).
- Aim of tumor CGP (methodology is NGS): **to find aberrations that can be targeted therapeutically**:
  - FoundationOne™ assay
    - is FDA-approved for solid tumors. It is based on 324 genes. All four types of genetic aberrations can be identified (substitutions, insertion, deletion and copy number alterations, as well as MSI and TMB) using paraffin embedded tumor sample. PDL1 testing can be added.
  - MI Transcriptome™ assay.
    - provides information on 592 genes, detects gene fusions and can differentiate fusions from other rearrangements in solid tumors. The assay is supposed to get FDA approval in late 2019.

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Do we have effective drugs for CUP patients?

a responsive subset:

favourable prognostic subset

- about 20% of CUP patients
- should be treated with primary-specific therapy corresponding to most likely primary site

an unresponsive subset:

poor prognostic subset

- about 80% of CUP patients

Int J Cancer 2014; 135, 2475–81.
Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Favourable prognostic subset

- Traditionally defined favourable subset:
  - women with isolated axillary adenopathy,
  - women with serous papillary peritoneal carcinomatosis,
  - squamous cell carcinoma involving mid-high cervical lymph nodes,
  - poorly as well as well-differentiated neuroendocrine carcinoma,
  - poorly differentiated and undifferentiated carcinoma (extra gonadal germ cell cancers),
  - men with blastic bone metastases and elevated PSA
  - patients with single, small and potentially resectable tumors
- Newly identified favourable CUP subset:
  - patients who look like CRC (CK 20 pos, CK 7 neg, CDX pos), should be treated as patients with advanced CRC (expected RR around 50% and mOS up to 3 years)

Abeloff's Clinical Oncology (6th Edition) 2020; Cancer of Undefined Site of Origin 1694-702.

Unfavourable prognostic subset (1)

- Sensitivity to chemotherapy is modest.
- GEP could identify ToO in majority of these patients.
  - If identified tissue specific therapy or inclusion into clinical trial (if available) is the best option.
  - If not-identified, the option is either clinical trial or CGP in terms to identify potentially treatable GA
    - in many countries expensive molecular assays are not available or not covered by insurance
    - targeted drugs and check point inhibitors are not covered by insurance
    - **at the time being we have no prove that such approach really influence patients' survival.** Data from well designed clinical trials are necessary.

Unfavourable prognostic subset (2)

- The majority of patients from this subset have poor prognosis.
- At presentation, two-thirds of patients have metastatic lesions in two or more visceral sites (most often liver, lung, lymph nodes and/or peritoneum).
- Patients are often in poor performance status.
  - For many of these patients BSC is the best option.
  - For selected patients empiric chemotherapy is justified.
  - Cisplatin or taxane-based doublets have been used, with little impact on survival.
  - Patients and relatives have to be informed that expected RR to ChT is only 20% to 30% and expected mOS not more than 9 to 11 mos. This might influence theirs' decision about treatment.

NCCN guidelines

Conclusions

- CUP is a heterogeneous disease with poor prognosis.
- It is mandatory to establish to which prognostic group the patient belongs to.
- In patients belonging to a favourable prognostic subset long-term survival can be achieved with appropriate treatment.
- Patients classified to unfavourable prognostic subset have to be informed about benefits and disadvantages of empiric therapy. Especially for patients with widespread disease and poor PS BSC is the best option.
- Novel approaches are promising, present a fundamental shift in the paradigm of treatment of cancer patients from tissue-specific to individual, patient customized treatment, directed according to tumor specific GAs.

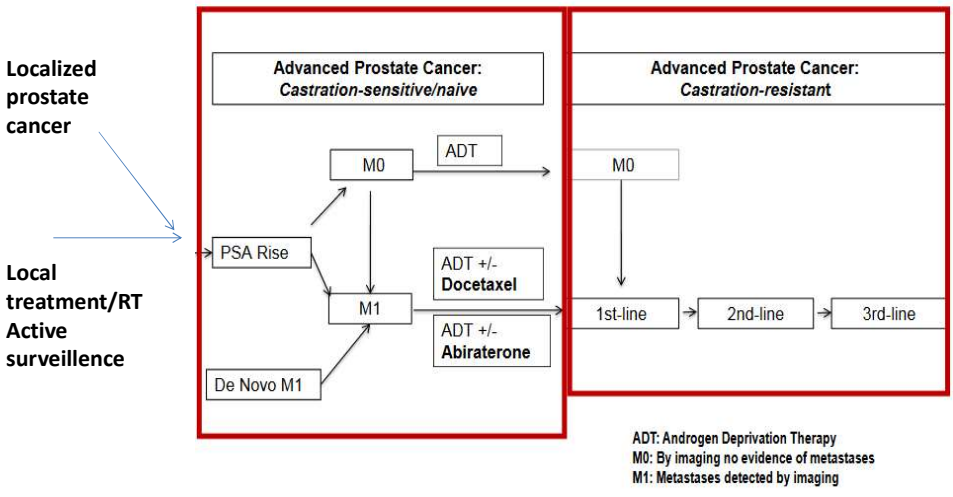
Systemic treatment of prostate cancer

Borislav Belev

Clinical Hospital Center Zagreb
School of Medicine Zagreb

1st Summer School in medical oncology –Ljubljana, 3.-6. September 2019

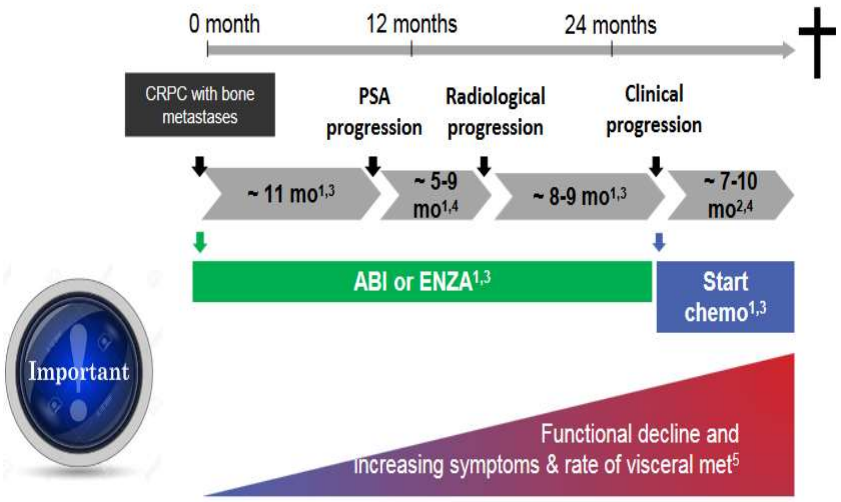
Prostate cancer – possible scenarios



Approved therapies for CRPC

ADT=androgen-deprivation therapy; mCRPC=metastatic castration-resistant prostate cancer.

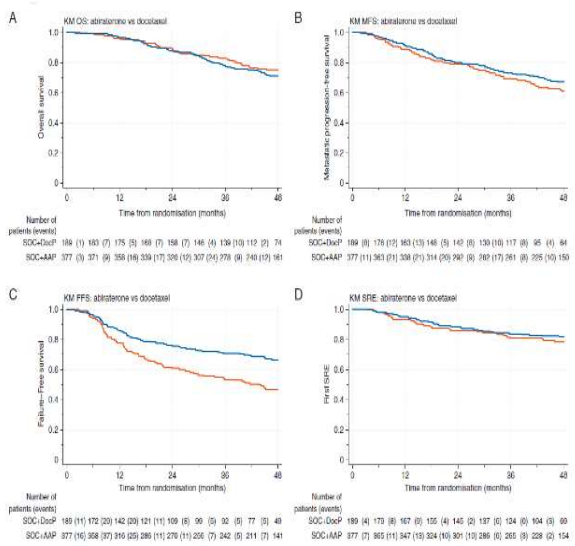
Time to events in the COU-AA-302 and PREVAIL studies

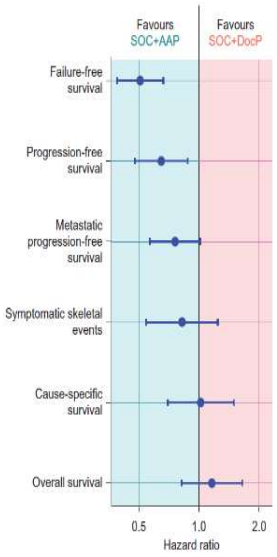


1. Ryan CJ et al. N Engl J Med 2013;368:138-48; 2. Ryan CJ et al. Lancet Oncol 2015;16:152-60; 3. Beer TM et al. N Engl J Med 2014;371:424-33; 4. Beer TM et al. Eur Urol 2017;71:151-4; 5. Pezaro CJ et al. Eur Urol 2014;65:270-3

Abiraterone or Docetaxel?

Directly randomised data from the STAMPEDE: 566 pts





Sydes et al. Annals of Oncology 29: 1235–1248, 2018

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 28, 2018 VOL. 378 NO. 26

Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer

Maha Hussain, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Per Rathenborg, M.D., Neal Shore, M.D., Ubirajara Ferreira, M.D., Ph.D., Petro Ivashchenko, M.D., Eren Demirhan, Ph.D., Katharina Modelska, M.D., Ph.D., De Phung, B.S., Andrew Krivoshik, M.D., Ph.D., and Cora N. Sternberg, M.D.

ORIGINAL ARTICLE

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Fred Saad, M.D., Simon Chowdhury, M.B., B.S., Ph.D., Stéphane Oudard, M.D., Ph.D., Boris A. Hadaschik, M.D., Julie N. Graff, M.D., David Olmos, M.D., Ph.D., Paul N. Mainwaring, M.B., B.S., M.D., Ji Youl Lee, M.D., Hiroji Uemura, M.D., Ph.D., Angela Lopez-Gitlitz, M.D., Géralyn C. Trudel, Ph.D., Byron M. Espina, B.S., Youyi Shu, Ph.D., Youn C. Park, Ph.D., Wayne R. Rackoff, M.D., Margaret K. Yu, M.D., and Eric J. Small, M.D., for the SPARTAN Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer

Karim Fizazi, M.D., Neal Shore, M.D., Teuvo L. Tammela, M.D., Ph.D., Albertas Ulys, M.D., Egils Vjaters, M.D., Sergey Polyakov, M.D., Mindaugas Jievaltas, M.D., Murilo Luz, M.D., Boris Alekseev, M.D., Iris Kuss, M.D., Christian Kappeler, Ph.D., Amir Snapir, M.D., Ph.D., Toni Sarapohja, M.Sc., and Matthew R. Smith, M.D., Ph.D., for the ARAMIS Investigators*

Take home messages

- Optimal sequence of treatment is not defined, since prostate cancer is heterogenous disease
- Treatment paradigm is changing dynamicaly, there are many new agents evolving in the last decade
- Androgen deprivation therapy is still fundamental
- Understanding of pathophysiology of disease determined new strategies, recognizing AR-pathway as still very important even in castrate situation
- Focus of treatment strategy is shifted toward earlier phases of disease, providing more benefitial outcomes
- Enzalutamide produces good therapy effect in mCRPC, abiraterone-acetat in mCRPC and mCSPC
- Docetaxel is valid option in mPC
- Cabazitaxel, mitoxantron and carboplatine are the options in mCRPC
- Apalutamide and enzalutamide are good option in m0CRPC
- New area of diagnostics – tumor genetic analysis – provides more individua-tailored treatment approach

Univerza v Ljubljani

Advances in treatment of renal cell carcinoma

Onkološki inštitut Ljubljana

Bostjan Seruga, MD, PhD

Division of Medical Oncology

Institute of Oncology Ljubljana and University in Ljubljana

Ljubljana, September 4, 2019

Topics

- Role of surgery in advanced RCC
- Targeted Therapy for Advanced RCC
- Immune Checkpoint Inhibitors for Advanced RCC
- Combination Therapy: Current and Future Opportunities
- Optimal Sequencing of Systemic Therapy in Advanced RCC
- Nuances in Treating Patients: Adjuvant Therapy, Treating Brain Metastases, Managing Adverse Events

Take-home Messages 1

- **The key for cytoreductive nephrectomy is patient selection**
  - **Cytoreductive nephrectomy should no longer be considered standard of care in intermediate- and poor-risk groups of metastatic RCC at least when medical treatment is required**
- **Radical metastasectomy followed by observation is commonly used strategy in selected patients with oligometastatic disease. There is no role of trageted agents in patients who underwent radical metastasectomy**

Take-home Messages 2

- **Small molecule targeted agents dramatically improved the outcome of patients with metastatic RCC**
- **Sequencing of small targeted agents should be based on the currently available evidence**
- **In the era of checkpoint inhibitors small molecule targeted agents remain important therapeutic strategy for patients with metastatic RCC**

Take-home Messages 3

- Anti–PD-1 based therapy is active in treatment-naive patients including favorable-risk patients
- Much, but not all, of the activity of nivo/ipi is likely from the anti–PD-1 component
- Anti–PD-1 monotherapy with nivo/ipi salvage might be a reasonable strategy when one is concerned about the toxicity of nivo/ipi
- A trial of nivo/ipi vs nivo in frontline RCC is indicated

Take-home Messages 4

- Most immune-related AEs are reversible with immunosuppression through steroid treatment
  - Typically start with high-dose IV and then taper over 1-3 mos
  - Exception: adrenal insufficiency and hypothyroid need replacement hydrocortisone and levothyroxine, respectively, without use of steroids
- No evidence that intervening with steroids curtails antitumor efficacy of agent

Take-home Messages 5

- **Adjuvant VEGF therapy, when adequately dosed, can offer very modest benefit balanced against toxicity**
- **The goal of a patient with newly metastatic RCC is potential cure; therefore, regimens with the highest chance of cure/durable response, balanced against acceptable toxicity/time off of treatment, should be prioritized**
- **Immunotherapy-based regimens offer the best chance of achieving patient goals**
  - **Whether immunotherapies in combination with one another or with VEGF therapies most effectively achieves these goals is as yet undefined**

IO–Non-IO Combinations

- **IO is different than tumor-directed therapy because of its ability to produce Treatment-Free Survival (TFS)**
- **Combinations that improve median PFS or median OS without producing TFS may sacrifice the potential of IO while contributing toxicity, inconvenience, and tremendous extra cost**
- **Not only must A+B > A followed by B (or B followed by A), but TFS must be maintained in order for such combos to be fully embraced**
- **Clinical trials with IO agents need to use IO endpoints**

ONKOLOŠKI INŠTITUT
INSTITUTE OF ONCOLOGY
LJUBLJANA

Naslov

Systemic treatment of bladder cancer

Marina Mencinger MD , PhD

International School for Medical Oncology
Ljubljana Sept 2019

Tumours of the urothelial tract

Cancer that starts in the urothelium is called urothelial (or transitional cell) cancer. By definition, urothelial carcinoma with divergent differentiation refers to tumours arising within the urothelial tract, in which some percentage of “usual type” urothelial carcinoma is present along with other morphologies

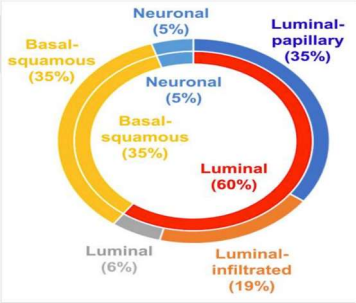
Histological type (1)	
Urothelial carcinoma	90-95%
Squamous-cell carcinoma	3%
Adenocarcinoma	2%
Small-cell carcinoma	<1%

Bladder Cancer (2)		
Superficial	pTa, pTis, pT1	75-85%
Muscle-invasive	pT2, pT3, pT4	10-15%
Metastatic	N+, M+	5%

1. Humphrey, European Urology 2016,
2. Matulay J, F1000Res. 2018;

Molecular characterisation of bladder c.

The TCGA (The Cancer Genome Atlas) study confirmed the existence of luminal (KRT20+, GATA3+, FOXA1+) and basal (KRT5,6,14+, GATA3−, FOXA1−) transcriptional sub- types, and neuronal subtypes-1.
The subtypes were associated with overall survival (retrospectively)-2.
Luminal-best OS, basal-most improvement in OS with NAC, claudine low-poor OS.



Using a novel single-patient subtype classifier based on The Cancer Genome Atlas identified 11 patients with a neuronal subtype, with 72% response rate to atezolizumab.-3

Rodriguez V Cancer Treat Res 2018; Seiler, Eur Urology 2017; Kim, Europ Urol., 2019

Muscular invasive bladder carcinoma has bad prognosis in comparison to muscular noninvasive

clasification	Stadium at diagnosis	Percentage of patients		5 year OS[1]	RIsk for relaps in 5 years
Muscular noninvasive	noninvasive (Ta, Tis ,T1)	51–75%[1–4]		96%	50–90%[2,4]
Muscular invasive	Localised (T2–4, N0)	35%[1]	30%[4]	69%	≈50%[6]
	Localy advanced (Tx, N1)	7%[1]		34%	
metastatic	(Tx, Nx, M1)	4%[1,5]		6%	NA

ISSUES!

1. Howlader N, et al. (eds). SEER Cancer Statistics Review, 1975–2011. **2.** NCCN Guidelines – Bladder cancer v1.2015. **3.** Sharma S, et al. Am Fam Physician 2009. **4.** Kaufman DS, et al. Lancet 2009. **5.** American Cancer Society 2014: Bladder Cancer. **6.** de Vos FY and de Wit R. Ther Adv Med Oncol 2010.

RATIONALE FOR NAC–prolonged OS: T2-4a, No, Mo: Neoadjuvant CT with platinum

Trial	n	Neoadj. CT + surgery vs. surgery alone
Meta-analysis 11 trials[1]	3.005	Statistically significant prolonged OS (HR=0,86; 95% CI: 0,77–0,95; p=0.003) • 5% absolute improvment 5 – y OS (from 45% na 50%)[2] Statistically significant prolonged survival without disease (HR=0,78; 95% CI: 0,71–0,86; p<0,0001) • 9% absolute improvement in 5 – y survival without disease

Recommended CT schemes by NCCN-2
3-4 cycles dd-MVAC : dose-dense metotreksat, vinblastin, doksorubicin in cisplatin)
4 cycles gemcitabin in cisplatin
3 cycles **CMV** (cisplatin, metotreksat, vinblastin)

1- Advanced Bladder Cancer Meta-analysis Eur Urol 2005 2-National Comprehensive Cancer Network. Bladder Cancer (Version 1.2019).

Rationale ACT: T3/4, N+, Mx: adjuvant CT

trial	n	Surgery + adjuv. CT vs surgery alone
Meta-analysis of 9 trials (1)	945	Statistically significant prolongation of OS (HR=0,77; 95% CI: 0,59–0,99; p=0,049) Statistically significant prolongation of survival withouth disease (HR=0,66;
EORTC (2)	284	PFS was longer with immediate versus deferred adjuvant chemotherapy [Hazard ratio (HR): 0.54; $p < 0.001$], but no diferences in OS were observed (HR 0.78; $p = 0.13$)

Randomised trials of adjuvant therapy are incomplete or underpowered.

1-Leow JJ, Eur Urol 2014; 2-Sternberg, Lancet Oncol 2015

Bladder sparing treatments : T2, No, Mo

Who are optimal candidates for bladder preservation?

Optimal candidates for bladder preservation with chemoradiotherapy include patients with tumors that present without hydronephrosis, are without concurrent extensive or multifocal Tis, and are <6 cm. Ideally, tumors should allow a visually complete or maximally debulking TURBT. See Principles of Radiation

1. TURBT + Concurrent chemoradiotherapy
2. Radiotherapy
3. TURB plus BCG

→ Reasses tumor status after 2-3 m

↓ Tumor present

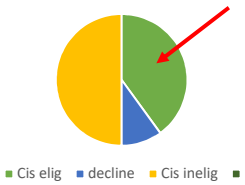
- CT
- CT+RT
- Paliative TURBT/salvage cystectomi
- BSC

Morales R, Clin Transl Oncol. 2011; NCCN guidelines 2019

1. Line treatment-cisplatin fit

The standard of care for first-line (1L) metastatic urothelial carcinoma (mUC) is cisplatin-based combination chemotherapy (NCCN V2.2019).

Eligibility for Cis NAC



Not eligible for cisplatin

ECOG PS 2	Baseline CrCl <60 mL/min	Hearing Loss Grade ≥2	Heart Failure Class III	Peripheral Neuropathy Grade ≥2

, NCCN guidelines, 2019 Galsky MD, et al. J Clin Oncol. 2011;

How do different cisplatin regimens compare (met or advanced bladder ca.)?

	GemCis	M-VAC	DD-MVAC	MVAC	DD Gem-Cis	DD M-VAC
mOS	=		=		=	
toxicity	<		<		<	
Quality of life	=		?		?	

ITT (263)	DD MVAC (6x)	MVAC (4x)	P-vrednost
5 y OS	21,8%,	13,5%	0,042
(RR)	72%	58%	0,016
Febrile neutropenia	10%	26%	0,001
(CR)	25%	11%	0,006

More ORR and CR.

von der Maase et al, J Clin Oncol, 2000; Sternberg et al, J Clin Oncol, 2001; Bamias, Ann Oncol., 2013, Sternberg et al, 2006, Eur J Can

1. Line (cisplatin ineligible or CT naïve in met setting))-NO randomised data!

		No	ORR all	DCR	ORR PD-L1 pos.	ORR in PD-L1 neg	mOS	Adverse events gr 3-4
Phase II, nonrandom, cohort 1 IMVIGOR 210	atezo	119	24% (CR 10%)		28% (CR 13%)	21 % (CR 8%)	16,3 m	18%
Phase II, nonrand Keynote 52	pembro	370	29% (CR 7%)	47%	51%	23%	11,5 m	16%

Eligibility for Cis NAC

1/3 to ½ pts are PD-L1 positiive

Balar , Lancet 2017. Vuky J, et al. ASCO 2018. Abstract 4524.; Balar AV, et al. ASCO 2018. Abstract 4523.

Why do we need PDL-1 positivity for first line?

EMA restricts use of Keytruda and Tecentriq in bladder cancer

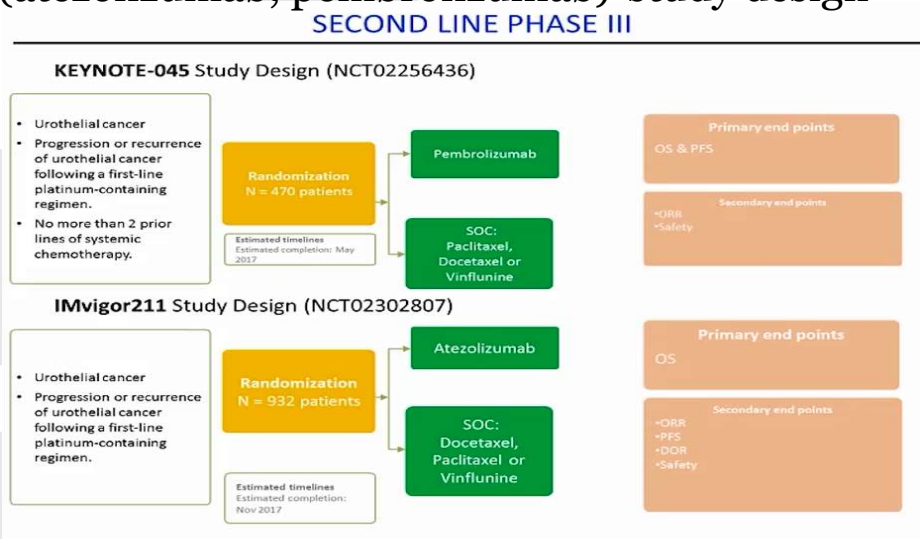
Data show lower survival in some patients with low levels of cancer protein PD-L1

Based on unreviewed data from rand. phase III trials. The results are not published yet.

PEMBROLIZUMAB:
Clone: 22C3
Combined positive score ≥10
the ratio of PD-L1–expressing **tumor-infiltrating immune cells relative to the total number of tumor cells**

ATEZOLIZUMAB:
Clone: SP142
staining on **tumor-infiltrating immune cells** covering at least **≥ 5%**

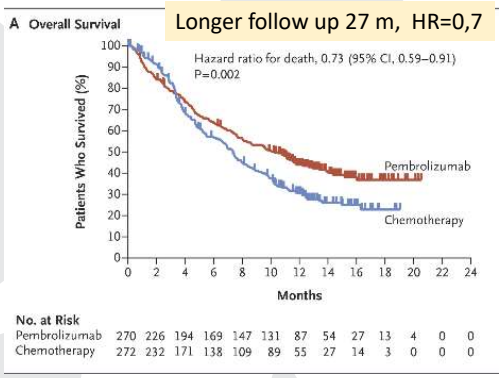
Second line phase III trials with PDL-1 inhibitors (atezolizumab, pembrolizumab)-study design



Bellmunt 2017, NEJM, Powels Lancet 2018

2.Line: Pembrolizumab vs CT: mOS and duration of response

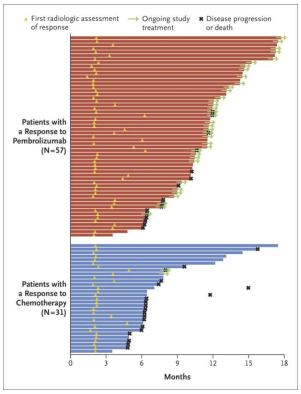
mOS



Longer follow up 27 m, HR=0,7

Duration of response

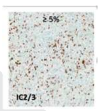
Response duration[2,3]		
Median in months (range)	Not reached (1.6+, 15.6+)	4.3 (1.4+, 15.4+)
Number (%[a]) of patients with duration ≥6 months	41 (78%)	7 (40%)
Number (%[a]) of patients with duration ≥12 months	14 (68%)	3 (35%)



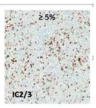
Time to Response and Duration of Response in Patients with a Confirmed Objective Response.

Bellmunt, NEJM, 2017

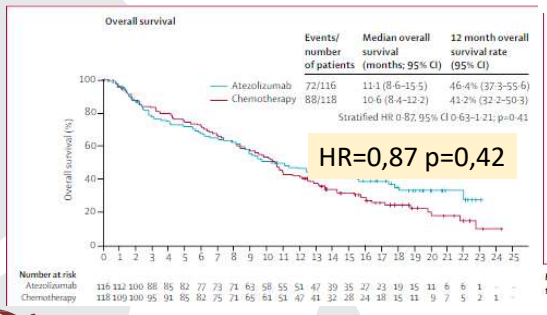
2. Line : Atezolizumab vs CT PDL1 positive patient group



mOS



Duration of response



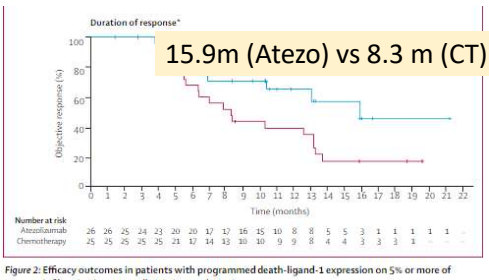
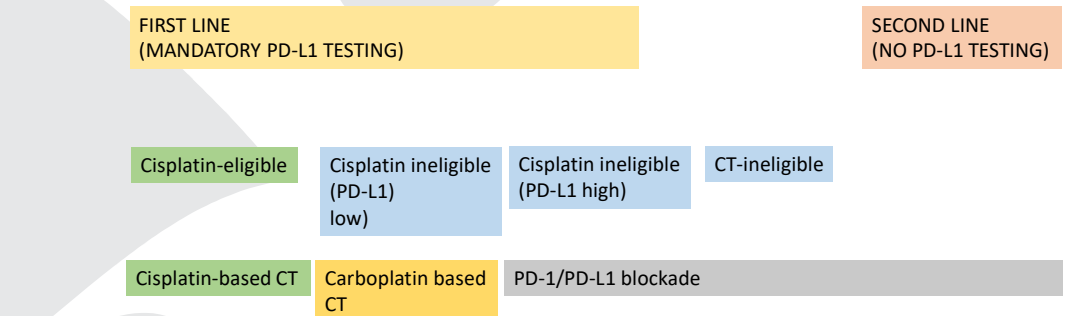


Figure 2: Efficacy outcomes in patients with programmed death-ligand-1 expression on 5% or more of tumour-infiltrating immune cells (IC2/3 population)

Powles, Lancet, 2018

Summary of Treatment in bladder cancer



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PALLIATIVE CARE
When to start and how to lead

Maja Ebert Moltara, MD
mebert@onko-i.si
Head of a Department for Acute Palliative Care
Department of Medical Oncology

ESMO Designated Centers of Integrated Oncology and Palliative Care

3-6 September 2019, Ljubljana, Slovenia

6 BASIC QUESTIONS:

WHAT?

For WHO?

WHO provides?

WHERE?

WHEN?

WHY?

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WHAT?

WHO definition of palliative care

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

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COMPREHENSIVE PALLIATIVE CARE

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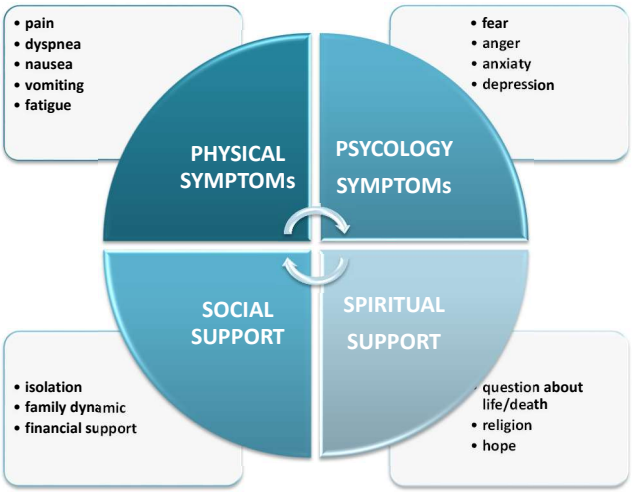
COMPREHENSIVE PALLIATIVE CARE



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WHO provides and WHERE?

All medical and non-medical members of teams in institutions where incurable patients are treated.

Basic palliative care (80% patient):
All levels of health system
(hospitals, community health centre, at home, senior homes, hospicih...)
All.

Specialied palliative care (20%):
Does not substitute basic palliative care, but it upgrade it for the patients with the most difficult and complex problems
Specialized teams (acute palliative care departent, mobile PC team)

EAPC: White Paper on standards and norms for hospice and palliative care in Europe

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CONTINOUS PALLIATIVE CARE

SENIOR HOMES

REGIONAL HOSPITALS

PATIENT WITH A FAMILY

FAMILY DOCTOR AND DISTRIC NURSE

EMERGANCY TEAM

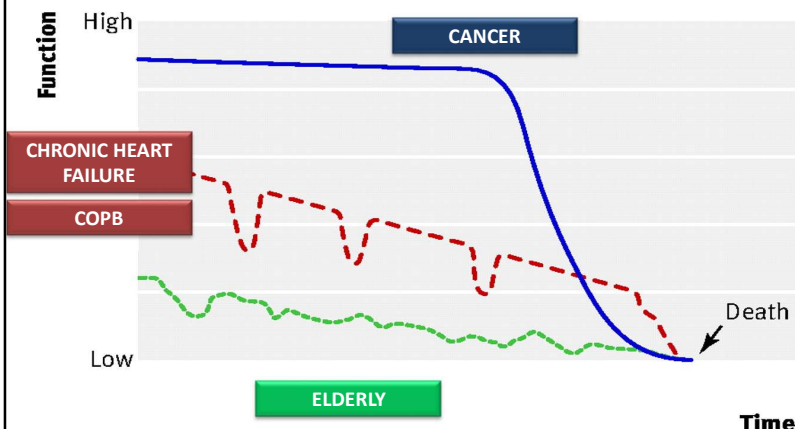
PC MOBILE TEAM

UNIVERSITY HOSPITALS

HOSPIC MOVEMENT

Hospic

For WHO?



Murray, S. A et al. BMJ 2008;336:958-959

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WHEN?

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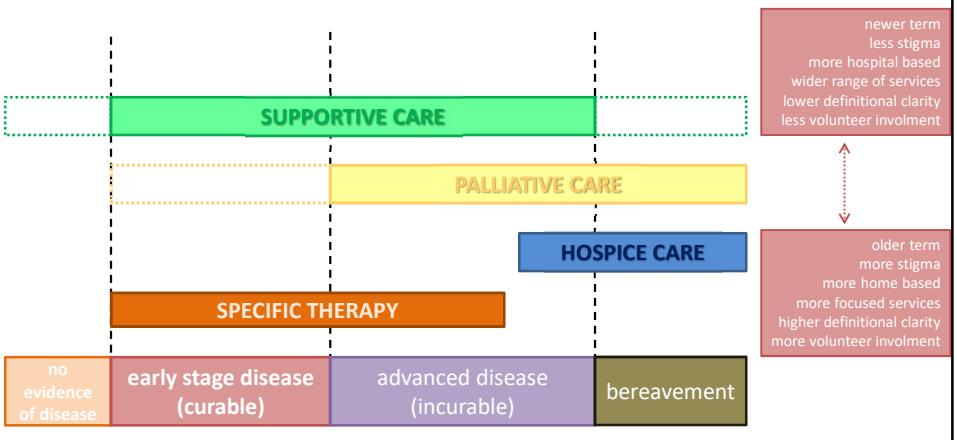
Conceptual framework



Hui, D. *et al.* Concepts and definitions for "supportive care," "best supportive care, " "palliative care, " and "hospice care" in the published literature, dictionaries, and textbooks. *Support. Care Cancer* 21, 659–685 (2013).

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WHEN?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H., J. Andrew Billings, M.D., and Thomas J. Lynch, M.D.

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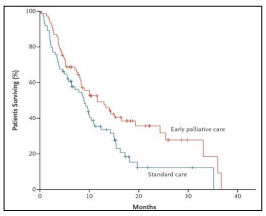
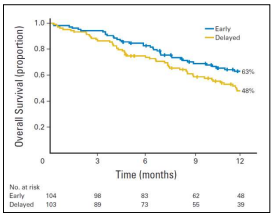
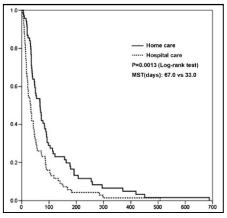
EARLY PALLIATIVE CARE



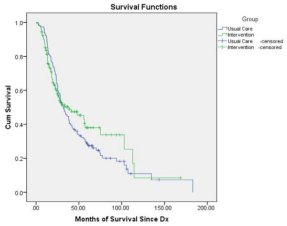
Temel, NEJM 2010



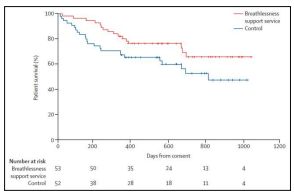
Bakitas, JCO 2015



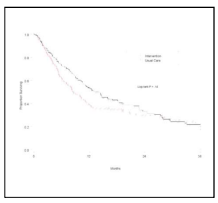
Murakami BMC Pall 2015



Ferell, J Pain Manag, 2015



Higginson 2015



Bakitas, JCO 2013

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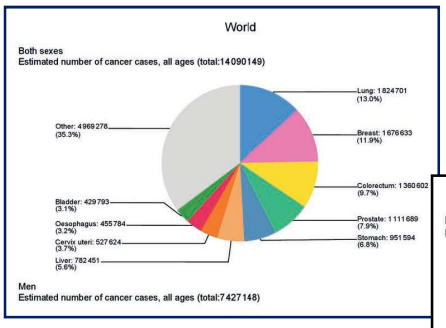
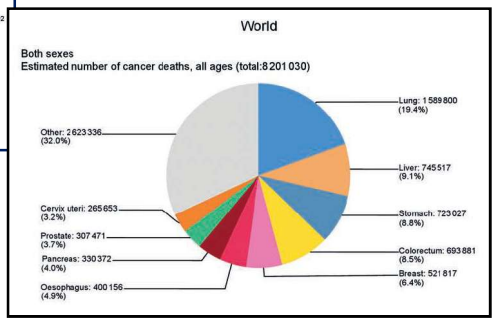
Extra: HOW many?





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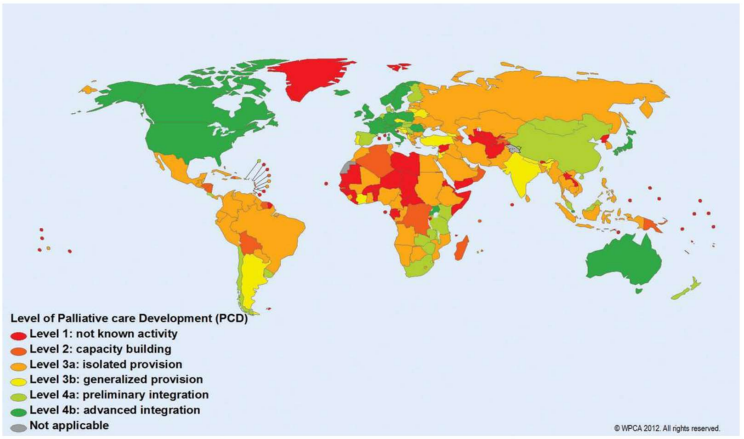
Global Atlas of Palliative Care at the End of Life, January 2014

Figure 1 World Map of Palliative Care Development 2011



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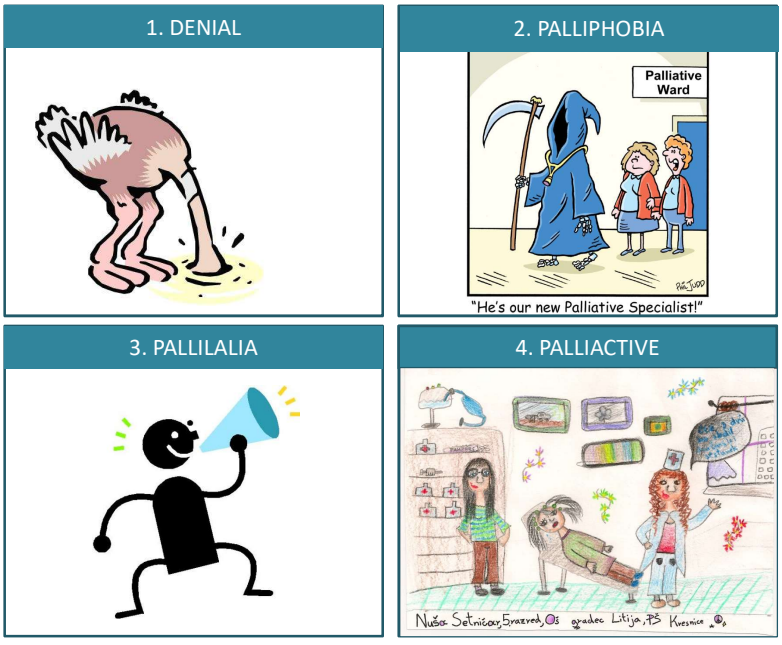

Top 10 Things Palliative Care Clinicians Wished Everyone Knew About Palliative Care

Jacob J. Strand, MD; Mihir M. Kamdar, MD; and Elise C. Carey, MD

2013 Mayo Foundation for Medical education an Research, Mayo Clin Proc. 2013; 88 (8):859865

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