

Advances in Metastatic / Secondary cancer

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June 2nd 2021

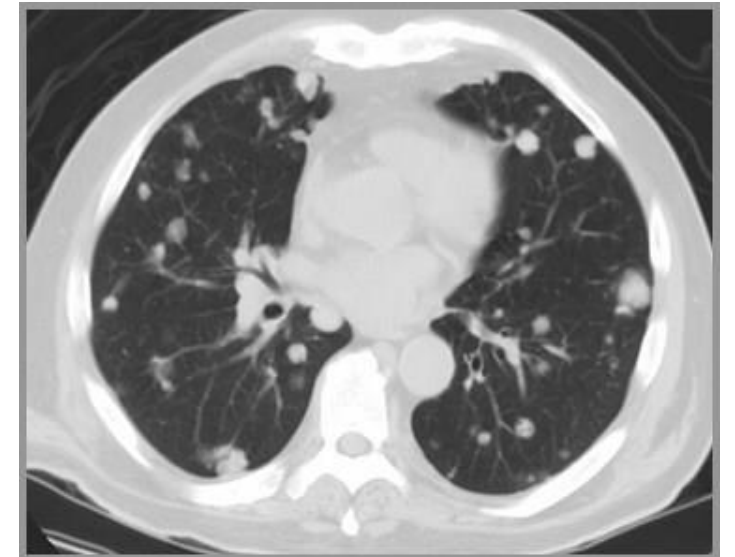
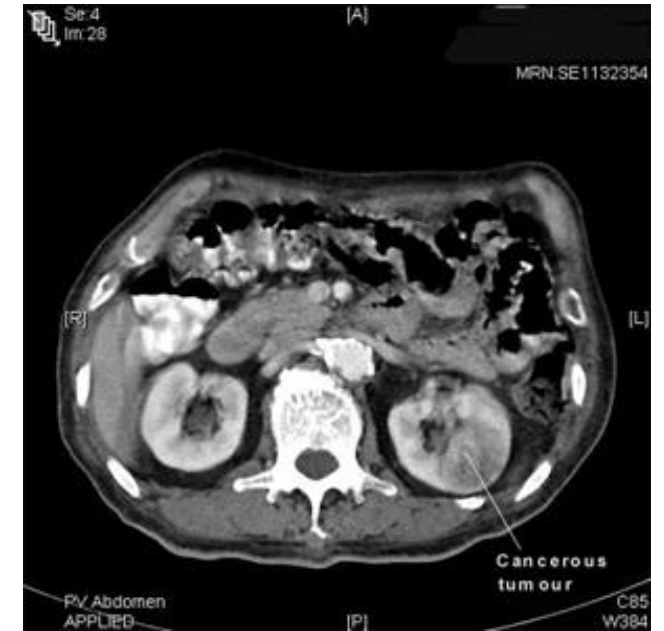
Outline of the talk

- Definition & Some facts
- How we devise a treatment plan
- Advances – how do they happen?
- New advances on available therapies
 - palliative care, surgery, radiation, ONCOLOGY
- Are there drawbacks to any of these advances?
- What else can YOU do?
- Q&A



What is metastatic / secondary cancer?

- Metastatic cancer is when cancer cells spread from a primary site to a different part of the body
- Metastatic cancers, down the microscope, are the same type of cancer as the primary site
 - Cancer cells can spread from kidney (primary site) to the lung (metastatic kidney cancer)
- Other names:
 - Advanced cancer
 - Stage IV cancer

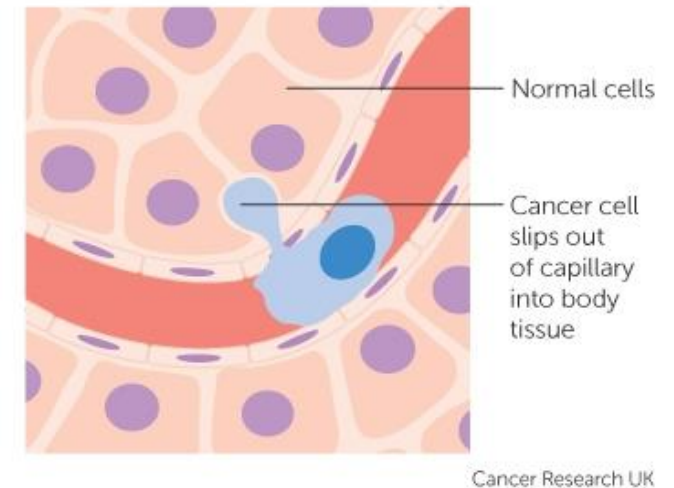
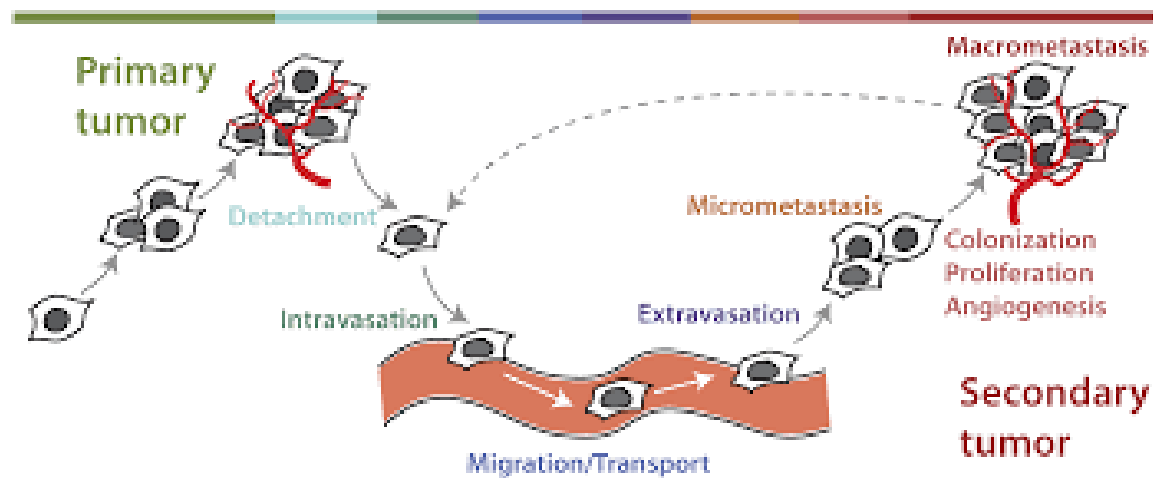


Difficult / Uncomfortable / Upsetting Facts

- Metastatic cancer is a frightening, difficult, challenging diagnosis / journey
- Sometimes it happens after a prior diagnosis of cancer / sometimes it's the first presentation of the cancer
- Sometimes it spreads to one part of one organ but often it's found to have to multiple places (one area in the liver v affecting multiple bones v multiple organs)
- In some cases, treatment can remove it
- In many cases, treatment can control it
- In many cases, it is incurable (one lives with it)

How does it happen / How does it spread?

- Dr Google: Metastatic cancer: 74 million results (0.48 seconds)
- Via the blood or the lymphatic system



- Avoiding the normal repair / warning mechanisms in the body (escape detection)

Diagnosis, Stage, Devising a treatment plan (MDT)

Diagnosis

Tests: biopsy, scans, assess main organs

Stage

Treatment planning*

This process takes time



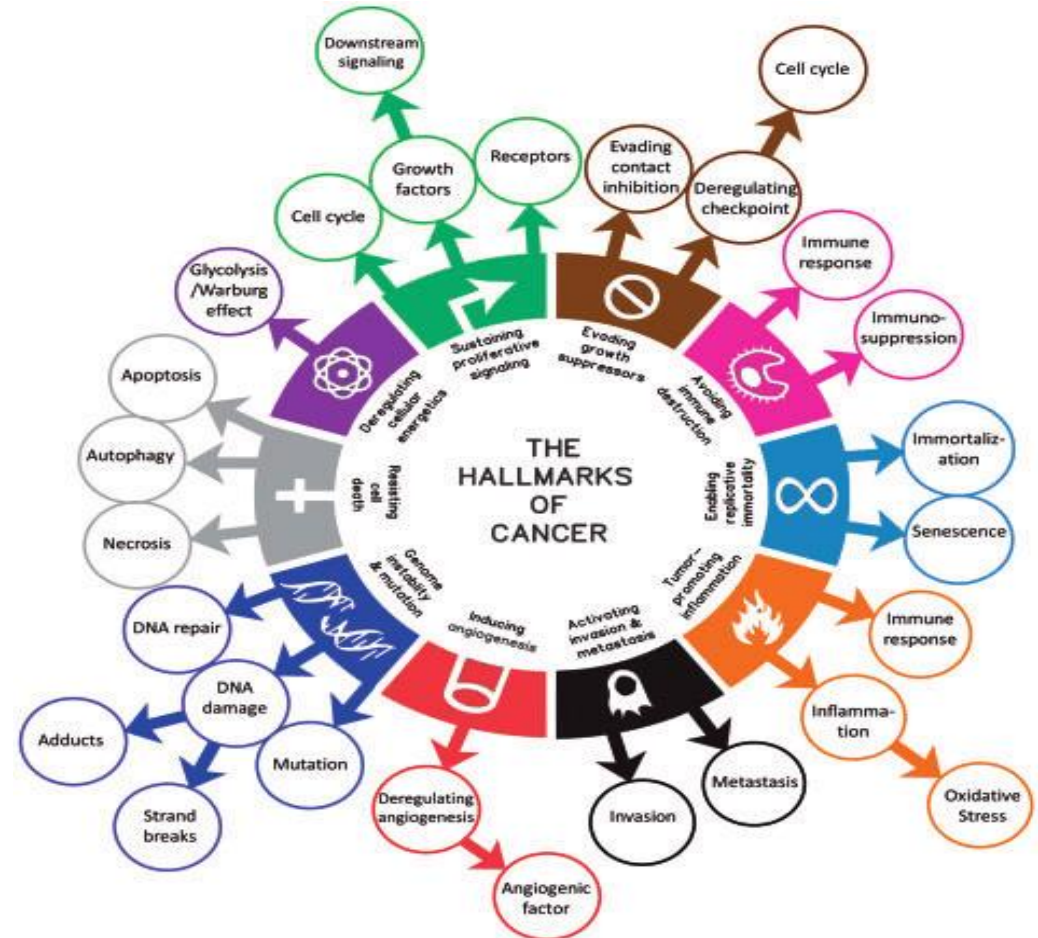
***MDT** = Multidisciplinary Team Meetings: Surgeon / Radiation Oncologist / Medical Oncologist / Pathologist / Radiologist / Specialist Nurses / Palliative Care Specialist / MDT Coordinator / Surgical and medical team members

Advances in treatments for Metastatic Cancer



How do advances happen? (Using process of drug development as an example)

- Problem: Advanced cancer
- Identify possible solution and assess it in a clinical trial
- Clinical trial process: “bench to clinic”
 - Lab studies - the science behind the possible solution



How do advances happen?



- Problem: Advanced cancer – New Drug
 - Testing in people – identify the effective & safe dose and it's side effects?
 - Testing in specific cancers – is it better than the current standard drug?
 - Licence – FDA EMA – if proven to be better (more effective) / safer than current standard therapy
 - Becomes available once it's licenced AND funded
- This takes time – we (and you) need to know will it work & what side effects might it cause
- What then?
 - Keep improving / as “resistance” arises – develop new drugs

Clinical Trials / Studies

- Current available therapies have been proven in clinical trials
- New studies provide early access to potential new treatments / combinations of therapies
- Not experiments
- Paperwork, time consuming, dot the “i’s” and cross the “t’s”
Your safety is paramount



What Advances are being made?





Palliative Care in Metastatic Cancer

Immediate responses when suggested:

- Fear
- You're giving up on me, I want another opinion
- Isn't that for people who are dying?



Palliative Care & Metastatic Cancer

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.

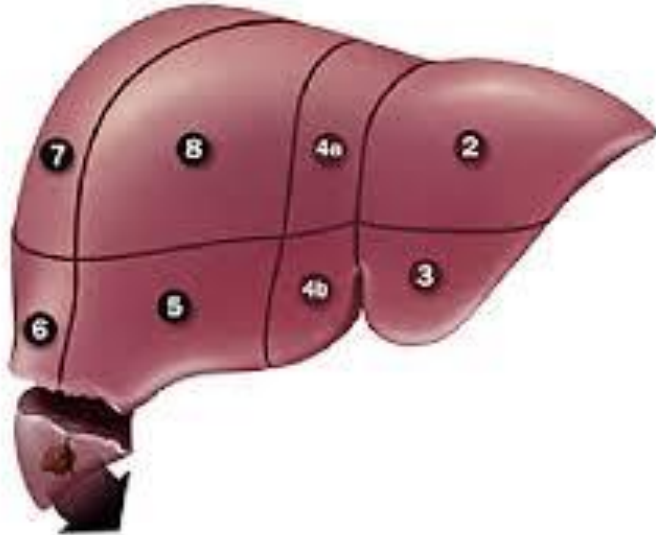
Temel, NEJM, 2010

- We suggest / recommend involvement of palliative care because we are aware that
 - it is so much more than “care of someone who is dying”
 - studies have shown that it improves survival in patients with advanced cancer
 - having this team involved in your care will improve cancer related symptoms
- If involvement with palliative care is offered – take up the offer

Advances in Surgical treatments in Metastatic Cancer

- I am not a surgeon / surgical oncologist
- I work with surgeons & surgical oncologists in Waterford, other cancer centres in Ireland and internationally
- Types of surgery: laparoscopic (shorter hospital stay & recovery)
- Indications: specific area (bone fracture / spinal surgery)
- Timing of surgery in metastatic cancer:
 - Drug therapy for a period of time & reassess (& rediscuss at MDT)

Surgical advances in Stage IV cancer



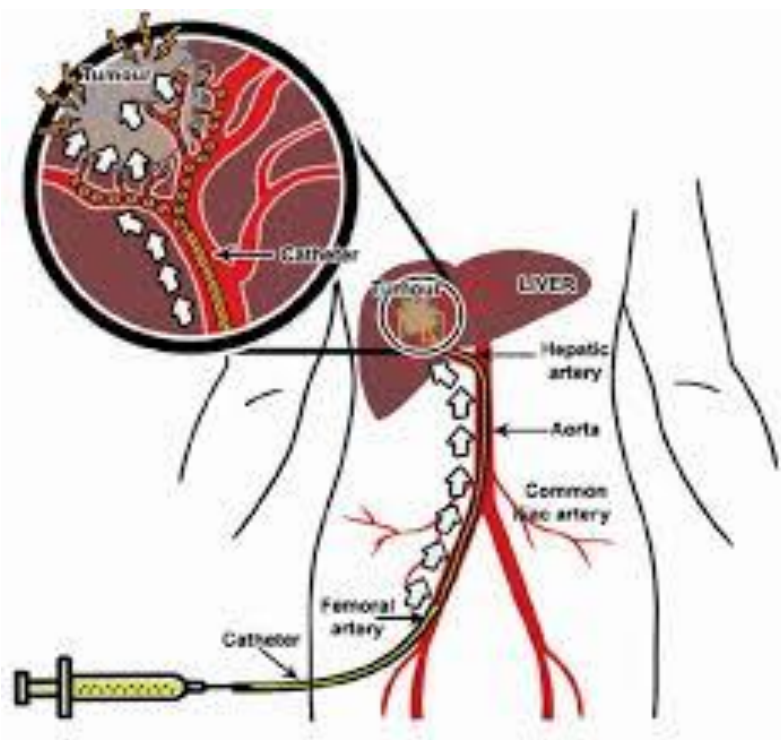
Orthopedic Surgical in Metastatic cancer



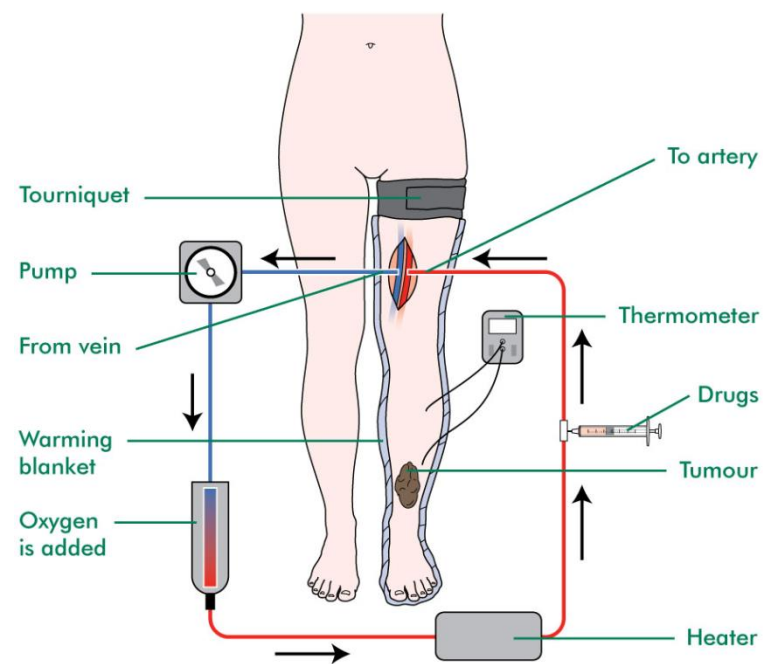
Other localized therapies in Metastatic Cancer

TACE

Transarterial chemoembolization



Isolated limb perfusion



Advances in Radiation Therapy

- I am not a radiation oncologist / specialist in radiation therapy
- I work within a team that includes radiation oncologists in Waterford, nationally & internationally
- Advances
 - Types of radiation therapy: Better targeting of tumour
 - Duration of radiation: Shorter durations (less side effects)
 - Repeat radiation: feasible pending the part of the body involved
 - Looking to achieve: Improve it's effectiveness, Reduce complications / side effects

Advances in Radiation Oncology - Available?

- 3D conformal radiation therapy
- IMRT: intensity-modulated radiation therapy
- Stereotactic radiation therapy
- Brachytherapy

- (Regular / standard / old-style radiation therapy remains the best therapy in many situations)

- YES available – multidisciplinary team working, discussion, planning

Radiation Therapy in Metastatic Cancer

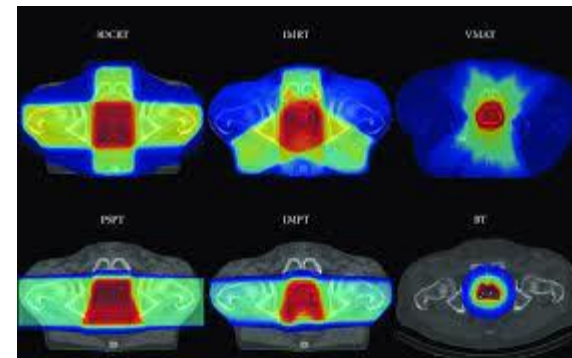
**Cyber knife / Gamma knife
(deliver stereotactic radiosurgery)**



Radiation planning / simulation



IMRT

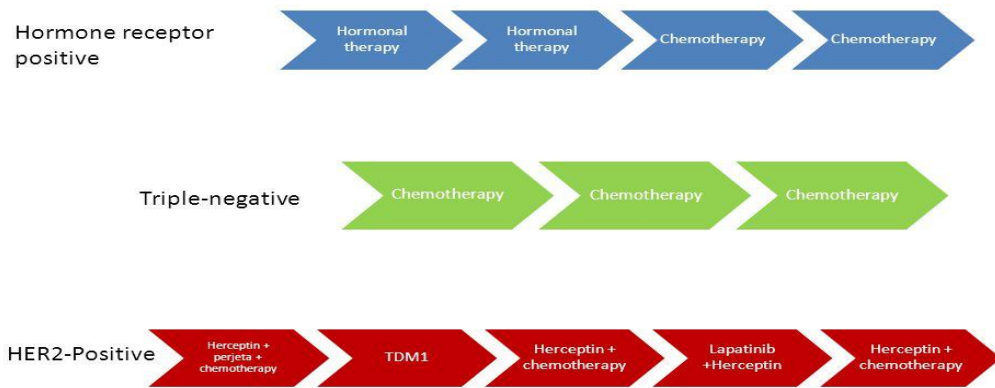


Oncology Treatment in Metastatic Cancer

“Lines” of Therapy

1st line – 2nd line – 3rd line – 4th line and so on

Treatment



*Note, these are just examples. Each patient is different and treatment is tailored accordingly.

Slide courtesy of Nancy Lin



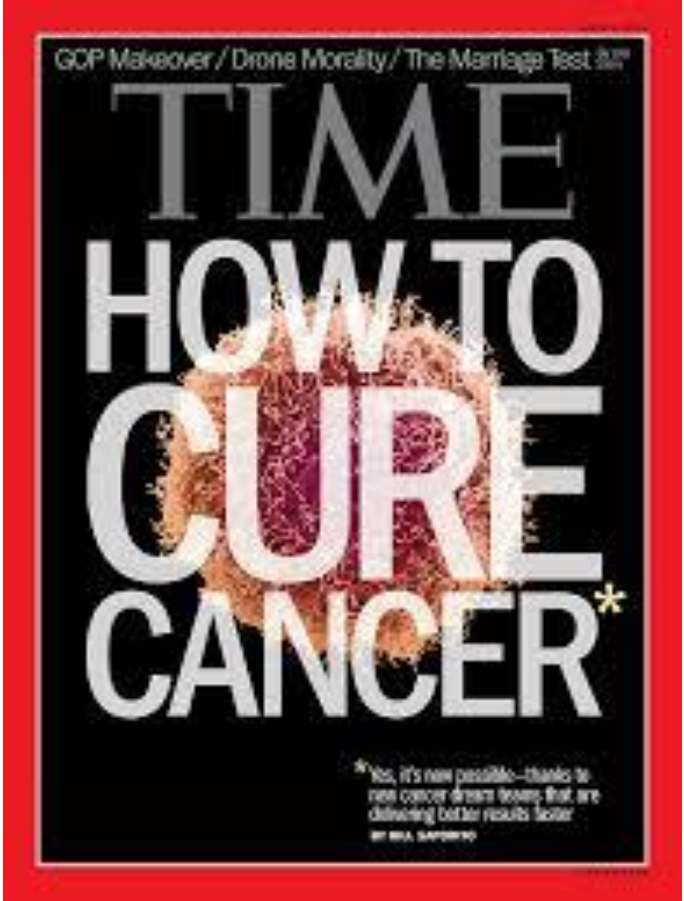
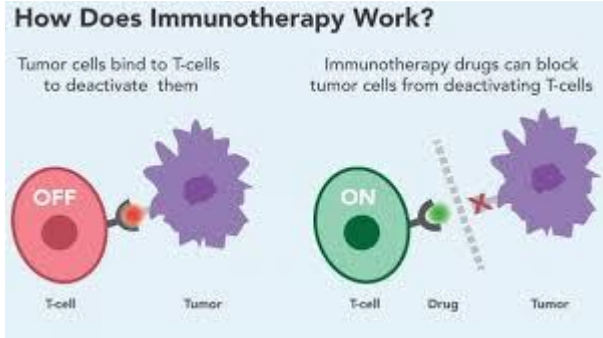
Oncology Advances in Metastatic Cancer

“Identify the driver / target”
Develop the anti-driver



Drug development: Identify the target / driver

- Target oestrogen / testosterone: Endocrine therapy (Breast & Prostate cancer)
- Target fast growing cells: Chemotherapy
- Target proteins / vessels delivering blood to tumour: HER2, EGFR, VEGF
- Target small molecules driving cancer growth: TKI's
- Target / boost immune system: Immunotherapy
- Target specific mutated genes involved in some tumours: PARPi
- Progress – new individual drugs / using drugs in combinations



Metastatic Melanoma

- Drug combinations
 - BRAF V600 mutation: Dabrafenib (BRAF inhibitor) & Trametinib (MEK inhibitor)
 - Ipilimumab & Nivolumab (immune checkpoint inhibitors)

Metastatic Kidney Cancer

- Drug therapy reduces the need for kidney cancer surgery
 - Sunitinib alone as effective as surgery followed by sunitinib
- Combination of drug therapies
 - Immunotherapy & TKI
 - Pembrolizumab & Lenvatinib
 - Avelumab & Axitinib
 - Immunotherapy combinations
 - Ipilimumab & Nivolumab

Metastatic Breast Cancer

- Triple negative:
 - Immunotherapy & Chemotherapy: Atezolizumab & Nab-Paclitaxel
 - Antibody-drug conjugate: Sacituzumab
- HER2 positive:
 - Trastuzumab deruxtecan
- Oestrogen positive:
 - CDK inhibitors with anti-oestrogen therapy
 - PIK3CA mutation - Alpelisib

Metastatic Lung Cancer

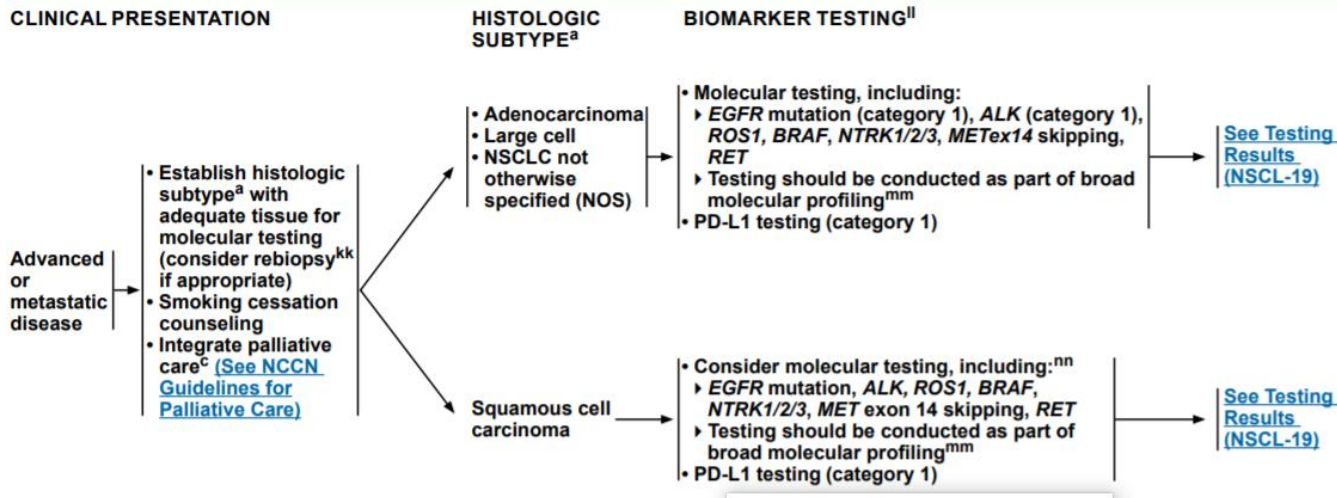
NCCN Guidelines Version 4.2021 Non-Small Cell Lung Cancer



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NCCN Guidelines Version 4.2021 Non-Small Cell Lung Cancer

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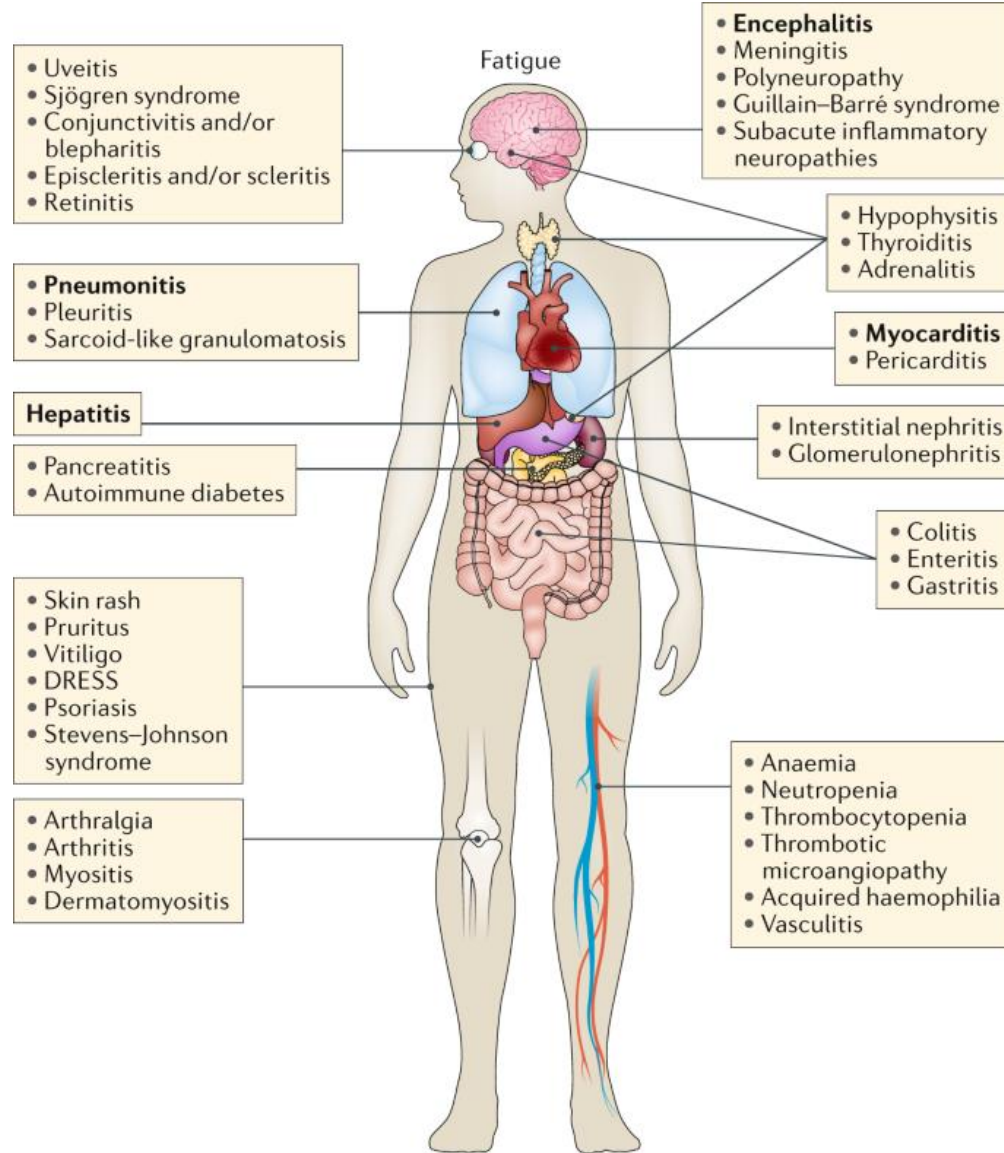
TESTING RESULTS^{kk,ll}

Sensitizing EGFR mutation positive	NSCL-20
ALK rearrangement positive	NSCL-23
ROS1 rearrangement positive	NSCL-26
BRAF V600E mutation positive	NSCL-27
NTRK1/2/3 gene fusion positive	NSCL-28
METex14 skipping mutation positive	NSCL-29
RET rearrangement positive	NSCL-30
PD-L1 ≥50% and negative for actionable molecular markers above	NSCL-31
PD-L1 ≥1%–49% and negative for actionable molecular markers above	NSCL-32
PD-L1 <1% and negative for actionable molecular markers above	NSCL-33

Are there drawbacks with these advances?

- Yes
- Side effects
- New issues
- What if it doesn't work / Stops working?

Immunotherapy Side Effects



How do we manage Immunotherapy Side Effects

- Being aware of them
- Educating **YOU** on what to watch for
- Educating our teams on what to watch for
- Specialist nurses
- Involve other specialities: endocrinologists, cardiologists, gastroenterologists, neurologists, hepatologists, dermatologists

What else? New Issue with Immunotherapy

- Chemo – scans show improvement (shrinkage), stable (no change) or progression (growth)
- Immunotherapy
- Experience / Multidisciplinary meetings: radiology & oncology expertise
 - Delayed response
 - Pseudo-progression (initial growth followed by shrinkage)

What happens when the treatment doesn't work or has a lot of side effects?



NOT WORKING = Cancer is growing (where we know it is or in new area)

- We stop the current treatment
- What's the next treatment?
 - How effective is it (in use or in clinical study)? Has it side effects?
 - Give time to consider the information
- What if the treatment is causing a lot of side effects
 - Alter the treatment (dose / schedule)
 - Treatment break



Clinical Trials

- Current available therapies have been proven in clinical trials
- Access to new treatments / combinations of therapies
- Not experiments
- Paperwork, time consuming, dot the “i’s” and cross the “t’s” Your safety is paramount



Advise when facing Metastatic Cancer

- Inform yourself with accurate information
 - Dr. Google is useful for general information but it's hard to find YOU
- It's a rollercoaster of a journey and you need teams of people
 - Family, friends
 - Medical team (Docs, Nurses, Hospital & Non-hospital based)
 - Be patient with the team as they develop the best plan for your situation

Oncologists have teams as well

- MDT within our own cancer centre
- ISMO: Irish Society Medical Oncology
- ESMO: European Society Medical Oncology
- ASCO: American Society Medical Oncology
- CTI: Cancer Trials Ireland
- International Trial Groups: BIG / EORTC / ETOP / NSABP / ANZGOG

The Future

- The work continues
- We (medics, nurses, pharmacists along with national and international colleagues) continue to make advances and bring them to you as safely & as quickly as we can

**Thank you and I'll finish the talk with these pictures
(can you spot the differences?)**

