Clinical Pearl

Patient: B. S., 51 years, male
Summer School Palliative Care 2019

<u>Admission to palliative care ward (19.07.2018):</u>

- Multimorbid and suffers from stenotic adenocarcinoma of the proximal colon, stage III, ECOG IV
- Severe septic shock with multiple organ failure as part of aspiration during anesthesia induction
- Bilateral pulmonary embolism
- Acute kidney failure
- Pneumonia due to aspiration
- fed enterally

Introduction

<u>Tumorboard (16.07.2018):</u>
Suggestion for best supportive care
Consilium was sent to palliative care

<u>Roundtable ICU visceral surgery:</u>
no further therapies (no surgery, no radiotherapy),
transfer to palliative ward suggested

In the beginning at palliative care ward

Subjective:

- very weak
- goal to get well and go home wants everything in an emergency
- agreed to proposal for an ACP consultation
- suspicious at the beginning of the inpatient stay and influenced by the events

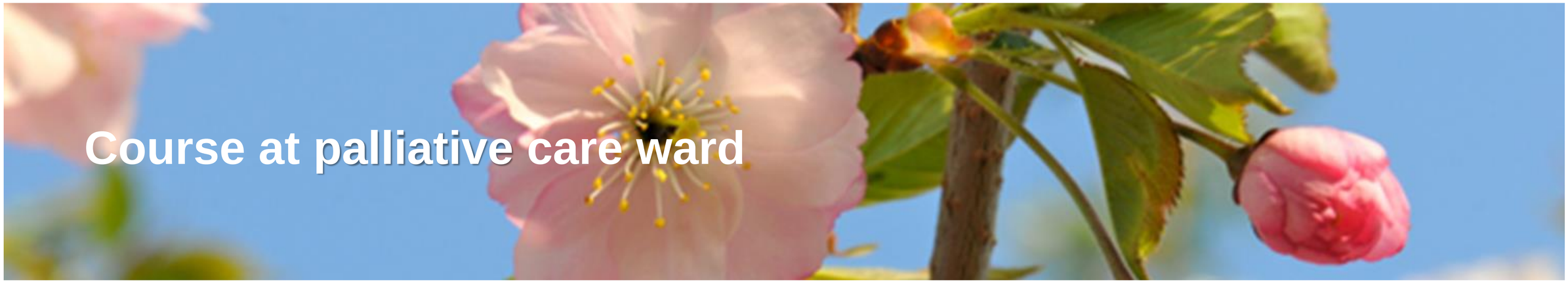
Objective:

- immobile
- massive leg edema with pruritus repeatedly malfunctioning dialysis catheters
- patient quickly distracted and reports of insults in the other department
- sometimes he is inadequate and mood-clouded

Involved therapies at palliative care ward

- Pastoral care (patient has 2 pastors who have already visited him)
- Psycho-oncology
- Social service for advice on long-term institutions and further administrative support
- Continuation of dialysis
- Roundtable with family
- Physiotherapy
- Nutritional therapy

During the stay: In the further course the patient showed himself affectionate, trusting and differentiated with the bad prognosis as well as the possibility of dying soon.



Course at palliative care ward

Subjective:

- over time appetite returned
- movement improved
- mood improved

Objective:

- receives regular dialysis (3 x per week)
- improvement of the retention values after stopping dialysis after failure of Shaldon catheter
- First Midazolam and Morphine-Boli for symptom control, over time not further needed

Procedure: Discharge to rehabilitation (3 weeks) and afterwards home

<u>Last Status:</u> Currently ECOG O, Last Neoadjuvant Chemotherapy as an outpatient Surgery planned for 28th of June 2019

USZ Universitäts Spital Zürich

University of Zurich[UZH]

ETH zürich

Bone-Pain-Samarium

Anna Beran-Kühne

Palliativzentrum Kantonsspital St. Gallen

Summerschool 27.Juni 2019

Mrs. T., 73 y

- **Adeno-Ca of the lung**, Dgn. 1,5 y ago

- multiple, disseminated osseous metastases, multiple brain metastases; EGFR Mutation

- Therapies:

  - EBRT, Xgeva

  - stabile under first line therapy with Iressa (Gefitinib=Tyrosin-Kinase- Inhibitor)

- **Chronically multitope pain-syndrome**

- degenerative spine alterations, spinal chord-stenosis, polyarthrosis, metastases..

Hospital admission

- **Symptoms:** Pain
- **Therapy:** Fentanyl TTS 100 mcg/h, Paracetamol+Metamizol 4x500mg, i.R.Effentora 200mcg 8/d, Effentora 400mcg 7/d

Screaming for her Effentora, depressive

Challenge:

Distinguish between Pain due to chronical pain syndrome, pain due to metastases, depressive symptoms, anxiety, impaired cognition, addiction

-> Fentanyl TTS 112mcg/h, Paracetamol4x500, Pregabalin 150 mg, Duloxetin 30->60mg. ,

i.R. Hydromorphon 2,6mg, Metamizol 4x1g

- **Symptoms:** Pain, Delirium

-> Halperidol, Rotation Fentanyl-> Hydromorphon

Symptoms: Pain, Delirium

Try something old – radionuclid-therapy

- **153 Samarium-EDTMP** (ethylene-diamine-tetramethylene-phosphonic acid) **Lexidronam** (Quadramet ®)
- Radiodiagnostic substance with effect on 99Tc bone scan-enhancing metastases
- Targeted «bone seeking» radioisotope delivery: low energy beta-particle (penetration 1-2 mm)
- binding hydroxyapatite, 5-fold increased uptake in lesions
- half life 46h, excretion renal

- Pain relief approved in breastcancer, prostatic cancer and lung cancer
- FDA-approved, not recommended by WHO
- Relief of pain in 60-80% within days, for at least 6-8 weeks
- Easy administration (intravenous once), ambulantWell tolerated – toxicity limited to myelosuppression (grade 0-II), Nadir 3-5 weeks
- combination with chemotherapeutics, bisphosphonates possible
- Repeated schedules without cumulation of myelosuppression

What happened to our patient?

- Relief of pain -> reduction of Hydromorphon, Haloperidol, stopp Duloxetin, Pregabalin. Regression of Delirium

- 2 Weeks after dismission:

- analgesy with Metamizol and Paracetamol on demand

- No delirium, mild cognitive impairment

What can we learn

- Less (oipioids) is more
- Sometimes try something different, something old
- Prefer targeted therapy if possible

What do You think?

Do You use radionuclid therapy?

Do you have other experiences?

- Breelyn A. Wilky, David Loeb: Beyond palliation: Therapeutic applications of 153 -Samarium EDTMP; Clin Exp Pharmacol 2013
- Oliver Sartor et al. Safety and Efficacy of repeat Administration of Samarium-153 Lexidronam to Patients with metastatic bone pain; Cancer 2007

- Alternativen: Rhenium, Strontium, Alpha-Strahler (Xofigo)-> keine Zulassung f. Sz Therapie
- Also effects in multiple myeloma, osteosarcoma…
- Flare-Phänomen within 72 hours
- Vorteile: Kurze HWZ (46 h), einmalige Gabe parenteral
- Kontraindikationen: manifeste Myelosuppression, Niereninsuffizienz (Krea >140 mmol/l), RT at same time
- Studien-Hinweise

Expert Rev Anticancer Ther. 2007 Nov;7(11):1517-27.

Samarium lexidronam (153Sm-EDTMP): skeletal radiation for osteoblastic bone metastases and osteosarcoma.

Anderson P[1], Nuñez R.

Author information

Abstract

Radiation therapy can be an effective means to treat bone metastases, which occur in more than 50% of cancer patients. (153)Samarium lexidronam ((153)Sm-EDTMP; Quadramet, Cytogen) is a radiopharmaceutical designed for deposition into bone metastases. Bone scans can identify patients that may benefit from targeted radiation therapy with (153)Sm-EDTMP. As an unsealed source of radiation therapy, (153)Sm-EDTMP is simple to administer: 1 mCi/kg is given in a similar fashion to a bone scan injection ((99m)Tc-MDP bone scan injection is given at 0.2-0.35 mCi/kg. Therefore, both are administered intravenously. However, the radiation-absorbed dose and radiopharmaceutical energy are different). Nevertheless, despite simplicity of administration, (153)Sm-EDTMP is underutilized for improving cancer pain in the skeleton. Repeated cycles and combined treatment with other modalities such as bisphosphonates, chemotherapy and/or external beam radiation are possible. (153)Sm-EDTMP combined with bisphosphonates, chemotherapy and/or radiation may provide better palliation of bone metastases and also in bone-forming tumors (osteosarcoma). Encouraging experience using high-dose (153)Sm-EDTMP for total marrow irradiation in hematologic malignancies involving the bones (e.g., myeloma or acute leukemia) is also reviewed.

PMID: 18020921 DOI: 10.1586/14737140.7.11.1517

Expert Opin Pharmacother. 2006 Aug;7(11):1475-86.

Samarium for osteoblastic bone metastases and osteosarcoma.

Anderson P[1].

Author information

Abstract

Samarium-153 lexidronam (153Sm-EDTMP) is FDA approved for painful osteoblastic bone metastases that image on bone scan. 153Sm-EDTMP decay has a therapeutic beta-emission and a gamma-photon for bone scan imaging. Monitoring of osteosarcoma radiation treatment effectiveness was performed with bone, CT, MRI and PET/CT fusion imaging. Bone scan and PET/CT improved in 5 out of 9 and 16 out of 18 osteosarcoma sites, respectively. 153Sm-EDTMP targets multiple sites of disease, with a single administration. Side effects of 153Sm-EDTMP (0.5-2.5 mCi/kg) have been minimal and include transient thrombocytopenia and neutropenia. 153Sm-EDTMP can be combined with radiation therapy, bisphosphonates and/or chemotherapy to synergistically improve palliation. This article reviews the rationale, indications and monitoring of standard-dose samarium and investigational high-dose 153Sm-EDTMP treatment of cancer involving bone.

PMID: 16859431 DOI: 10.1517/14656566.7.11.1475

[Indexed for MEDLINE]

Palliative treatment of metastatic bone pain with radiopharmaceuticals: A perspective beyond Strontium-89 and Samarium-153.

Guerra Liberal FDC[1], Tavares AAS[2], Tavares JMRS[3].

Author information

Abstract

PURPOSE: The present review article aims to provide an overview of the available radionuclides for palliative treatment of bone metastases beyond (89)Sr and (153)Sm. In addition, it aims to review and summarize the clinical outcomes associated with the palliative treatment of bone metastases using different radiopharmaceuticals.

MATERIALS AND METHODS: A literature search was conducted on Science Direct and PubMed databases (1990 - 2015). The following search terms were combined in order to obtain relevant results: "bone", "metastases", "palliative", "care", "therapy", "treatment", "radiotherapy", "review", "radiopharmaceutical", "phosphorus-32", "strontium-89", "yttrium-90", "tin-117m", "samarium-153", "holmium-166", "thulium-170", "lutetium-177", "rhenium-186", "rhenium-188" and "radium-223". Studies were included if they provided information regarding the clinical outcomes.

RESULTS AND CONCLUSIONS: A comparative analysis of the measured therapeutic response of different radiopharmaceuticals, based on previously published data, suggests that there is a lack of substantial differences in palliative efficacy among radiopharmaceuticals. However, when the comparative analysis adds factors such as patient's life expectancy, radionuclides' physical characteristics (e.g. tissue penetration range and half-life) and health economics to guide the rational selection of a radiopharmaceutical for palliative treatment of bone metastases, (177)Lu and (188)Re-labeled radiopharmaceuticals appear to be the most suitable radiopharmaceuticals for treatment of small and medium/large size bone lesions, respectively.

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J Bone Miner Metab. 2014 Jul;32(4):434-40.

Palliative treatment of bone metastases with samarium-153 EDTMP at onset of pain.

Gallicchio R, Giacomobono S, Nardelli A, Pellegrino T, Simeon V, Gattozzi D, Maddalena F, Mainenti P, Storto G.

Abstract

We evaluated the pain response and daily discomfort in patients suffering from a borderline degree of bone pain due to breast or lung cancer bone metastases, who had undergone early palliative radionuclide treatment. The results were compared with those from patients who had received standard analgesic therapy. Twenty-one patients (65.7 ± 3 years; 17 women) with metastatic bone cancer underwent samarium-153 (Sm-153) ethylene diamine tetramethylene phosphonate (EDTMP) administration (group A) and 18 patients (64.3 ± 8 years; 16 women)continued to receive standard analgesics (group B; control group). The patients kept a daily pain diary assessing both their discomfort and the pain at specific sites by means of a visual analog scale, rating from 0 (no discomfort–no pain)to 10 (worst discomfort–pain). These diaries were reviewed weekly for 2 months and three physicians rated the pain response on a scale from -2 (considerable deterioration) to +2 (considerable improvement). Baseline characteristics were similar in both groups. The reduction of total discomfort and of bone pain in group A was significantly greater compared to group B ($p < 0.0001$). A significant improvement of clinical conditions was observed in group A, where the physician rate changed from -1 to 1, compared to group B in which the rate changed from -1 to 0. Sm-153 EDTMP therapy can be considered for patients with bone pain from breast and lung cancer in advance, i.e.,before the establishment of severe pain syndrome.

J Clin Oncol. 1989 Dec;7(12):1926-31.

A phase I study of samarium-153 ethylenediaminetetramethylene phosphonate therapy for disseminated skeletal metastases.

Turner JH[1], Claringbold PG, Hetherington EL, Sorby P, Martindale AA.

Author information

Abstract

Thirty-five patients with disseminated skeletal metastases from a variety of tumor types underwent clinical trial of samarium-153 ethylenediaminetetramethylene phosphonate (153Sm-EDTMP) on a day-patient basis. Individual beta radiation dosimetry was based on pharmacokinetic studies of a 20 mCi tracer dose of 153Sm-EDTMP. The retained skeletal activity varied unpredictably from 40% to 95% of the administered dose, but in all patients greater than 98% of the nonosseous activity was cleared in the urine within 6 hours. Prospective calculation of radiation dosimetry in each patient permitted an accurate dosage schedule based upon total red marrow exposure, starting at 100 cGy and escalating to 280 cGy to define the dose-limiting myelotoxicity. Pain was relieved in 22 of 34 evaluable patients (65%) for periods ranging from 4 to 35 weeks, following a single administration of 153Sm-EDTMP. Recurrence of pain responded to retreatment with 153Sm-EDTMP in five of nine patients. The dose-limiting toxicity was myelosuppression manifested particularly by delayed thrombocytopenia. Platelet counts less than 100 x 10(9)/L occurred in 42% of courses when bone marrow radiation absorbed dose exceeded 200 cGy. Myelosuppression was transient and platelet counts had recovered to pretreatment levels within 10 weeks of treatment. 153Sm-EDTMP is effective for the amelioration of pain due to disseminated skeletal metastases particularly with carcinoma of breast or prostate where 83% of patients experienced pain relief. In 15 of the 34 evaluable patients there was evidence of stabilization or regression of skeletal metastases on radiographs and follow-up technetium-99m methylene diphosphonate (99mTc-MDP) bone scans.

Comment in

Radionuclide targeting of bone metastases: which efficacy? [J Clin Oncol. 1990]

Pearl

Christine Zobrist

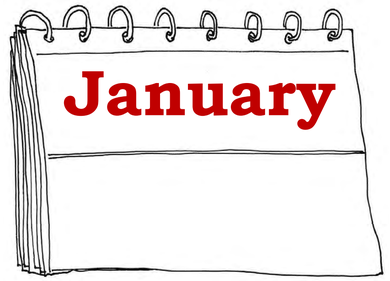
Kantonsspital Baselland

Mrs Monty

Mrs Monty

- 32 yrs young
- Married, mother of three children (½-5 yrs)
- Resources
  - family, friends
  - faith
  - work

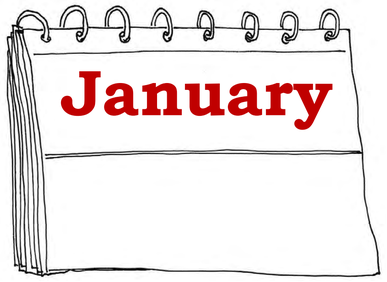
Mrs Monty



- Pressure - cheek left
  - GP several times - trivialized
- Diagnosis:
  - MR: tumor maxillaris left → Bi
  - Undifferentiated cancer sinona
- Therapy:
  - Huge surgery
  - curative!

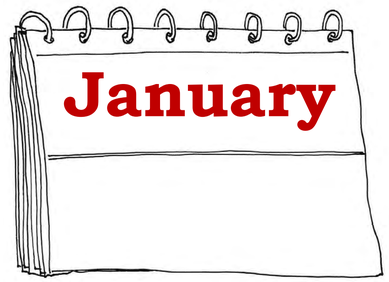
room 206

First contact



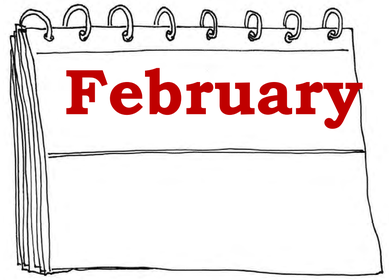
- Before surgery
- ‘~~Palliative Care~~’ → symptom control
- Get to know each other
- Practical stuff
- Advance directive

Before surgery – in hospital



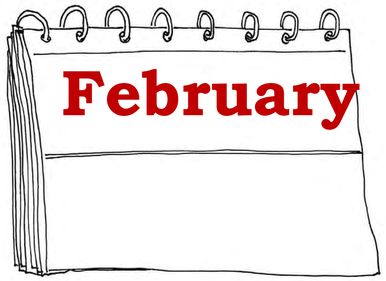
- Advance directive
  - Tracheostoma
  - Changes in body
  - Passed illnesses, symptoms
  - children
- ‘Agreements’
  - Visits – length, goals…
  - Family contacts
  - communication – yes/no

Surgery



Orbitomaxillektomie, extraction of teeth, Tracheotomy, neck dissection left, stomach tube, tubus in vestibulum nasi left

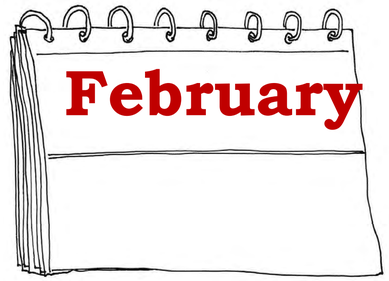
Postoperative – in hospital



- Happy, ‘everything’ was over
- Big changes in body image
  - Husband and children
- Symptom control
  - pain
  - breathlessness
  - nausea
  - Troubles sleeping
- Discussions about further therapies
  - a

    Körperveränderungen schon so ausgeprägt, kann ich mir nicht schlimmer vorstellen
  - Chemo nein

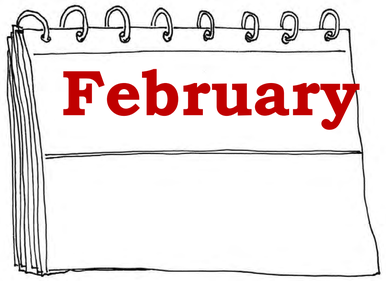
    die Langzeitnebenwirkungen kann ich mir nicht vorstellen



‘You know, the oncologist war here. He talked to me with a lot of time, he explaned everything to me. I don’t think he forgot anything.
He ‘served’ me all the information like on a tray, that stayed between us’

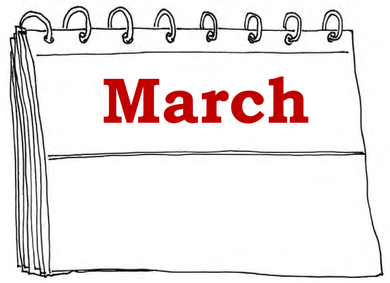
‘the otorhinolaryngologist talked to me about possible further procedures as well. He mentioned statistics and potential side-effects.
Sometimes it felt, as if he sat next to me on my bed, as if he didn’t tell the facts in regard of my cancer, but in regard of me. That was a big help…’

After surgery – in hospital



- Happy, ‘everything’ was over
- Big changes in body image
  - Husband and children
- Symptom control
  - pain
  - breathlessness
  - nausea
  - Troubles sleeping
- Discussions about further therapies
  - Radiotherapy yes
    changes in body image already huge
  - Chemotherapy no
    longterm side affects

Outpatient consultations - ORL

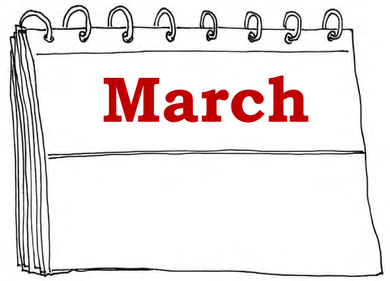


- Doing well
- Analgesia complex
- Discussions about changes in body image

  and role in family

  - Regular consultations with the psycho-oncologist

Outpatient consultations – ORL

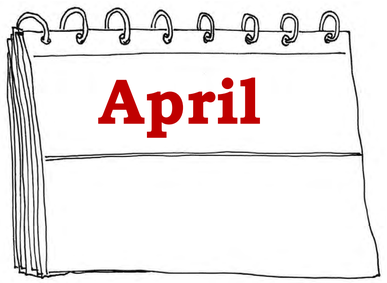


- Radiotherapy planned
- Metastasis? Lymphogenous, lungs
- Further examinations needed
- Radiotherapy not started
- Discussion with Mrs and Mr Monty:
  - ORL-doctor
  - Patient and husband had many clear ques
    st answers

It's impossible my wife dies at home!

discussion the husband looked at me:

Outpatient consultation



- Diagnosis: Metastasis in several lymphnodes and lung

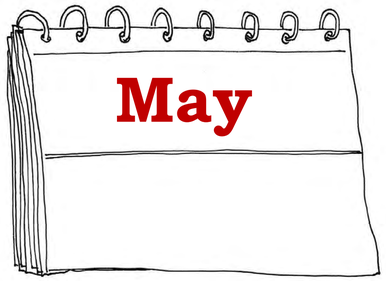
  Hospitalisation für Wedge-Resektion
- Now Chemotherapy und Radiotherapy
- Progress: Change from Chemotherapy → Immunotherapy

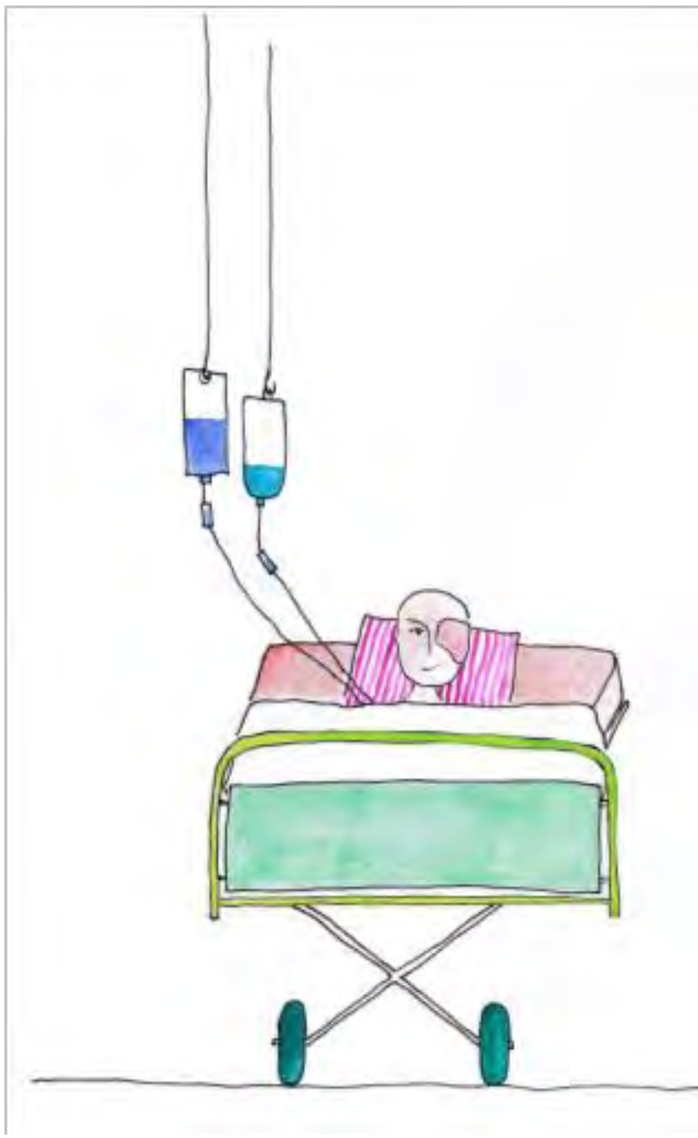
  Radiotherapy continued
- Patient and husband realistic, ready to fight

  Couple: open communication about illness, changes in body image
- Symptom-control difficult

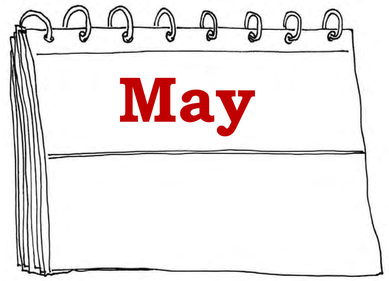
Hospitalisation – ORL

- fatigue
- weekness
- pain
- ‘I’m not myself’, ‘I’m loosing myself’



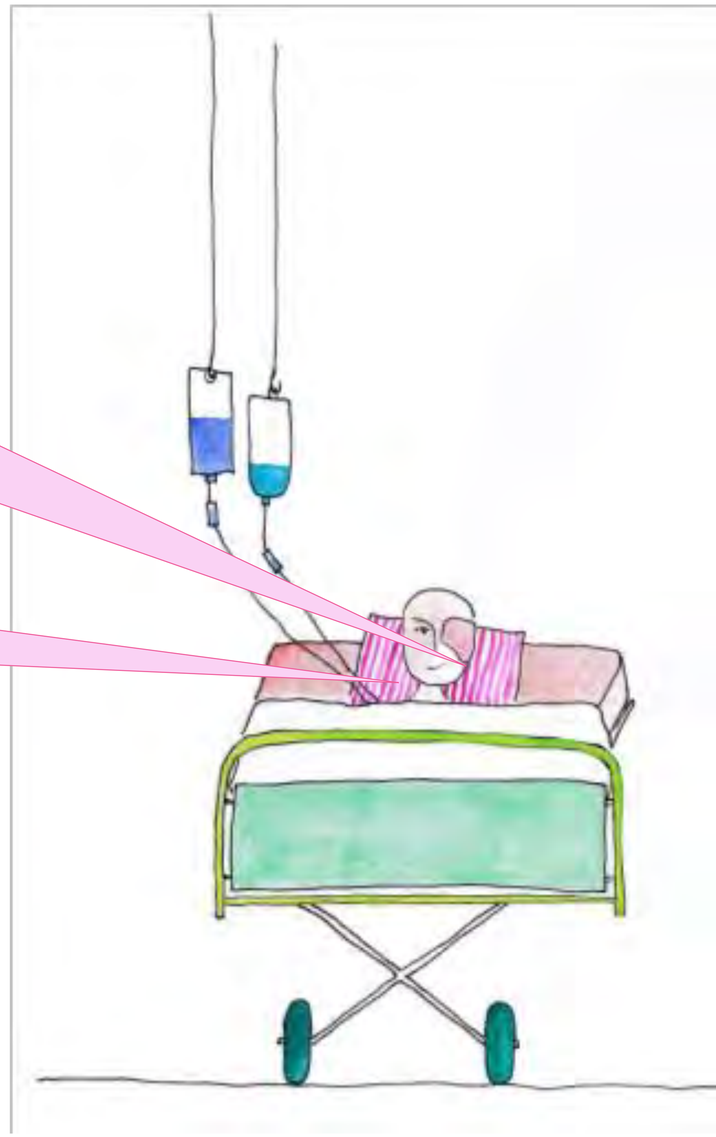


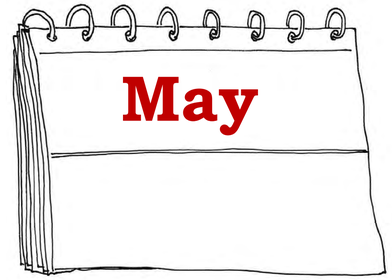
Existential crisis



‘what more suffering waits for me?’

‘I’m here and I’m loosing my role as a mother.
I consist only of illness.’





‘I believe in God and I asked a priest to come. I can’t make sense of my story.’

‘All by the sudden my suffering is bigger than my religious faith’

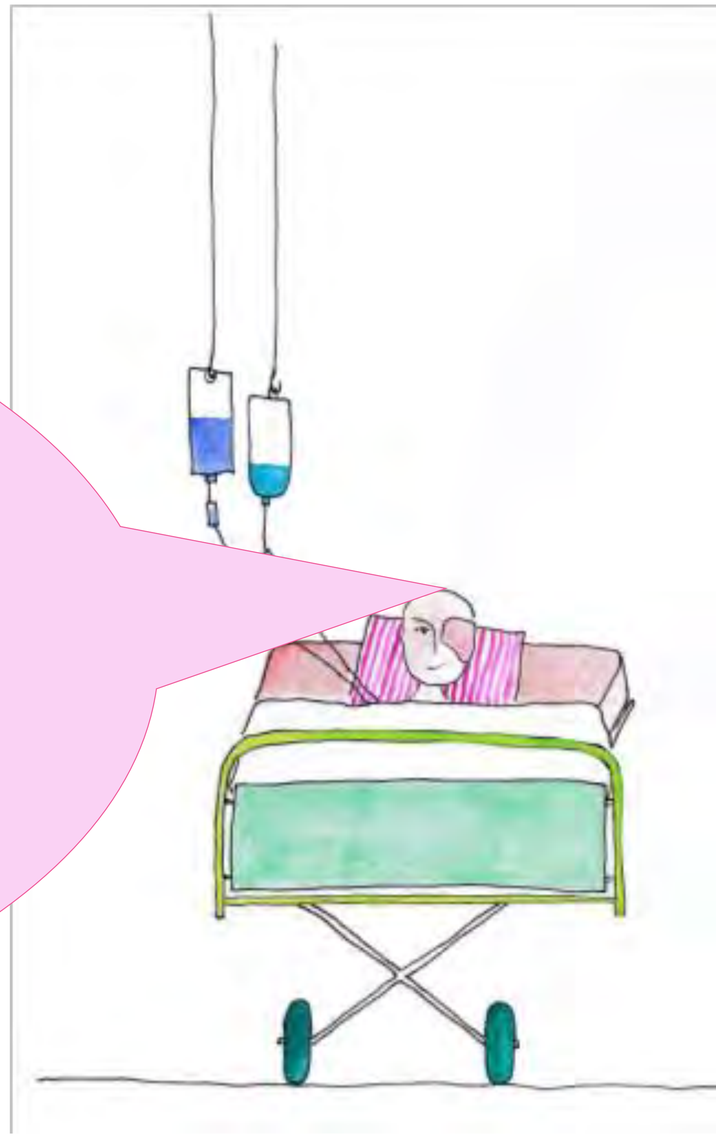
‘There is a higher mission in heaven, that waits for you’

‘…what higher mission is there than being a mother? What might possibly be so important that I have to leave my children behind?’

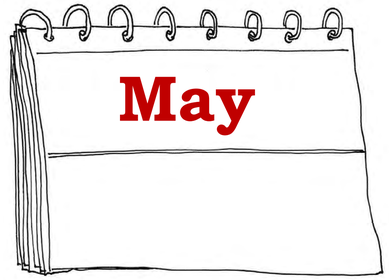
‘…I am loosing my faith at a point in time, when I thought it would carry me…’

Wish to die

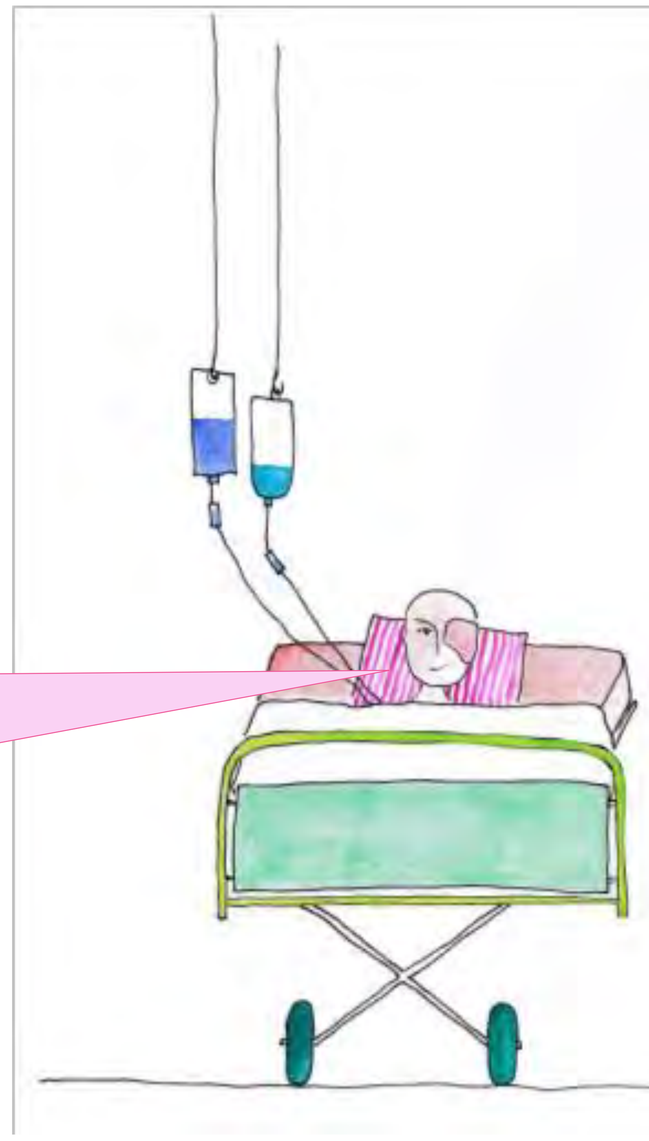
‘I would like to talk about Exit with you. I want my husband to be here to. I want to know everything about it.
I’m afraid to get to a point when I’m not able to function anymore – but still have to keep going’

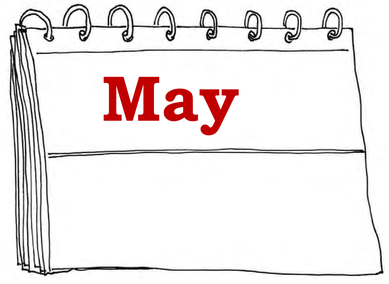


Sedation



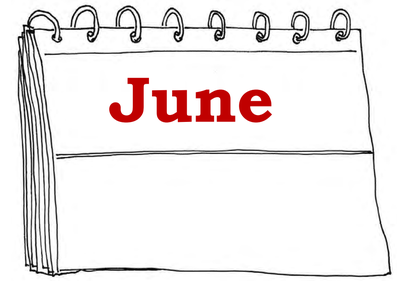
‘A friend of mine told me, that it is possible to just sleep, if I’m at the end of my strength.
Is that true?’





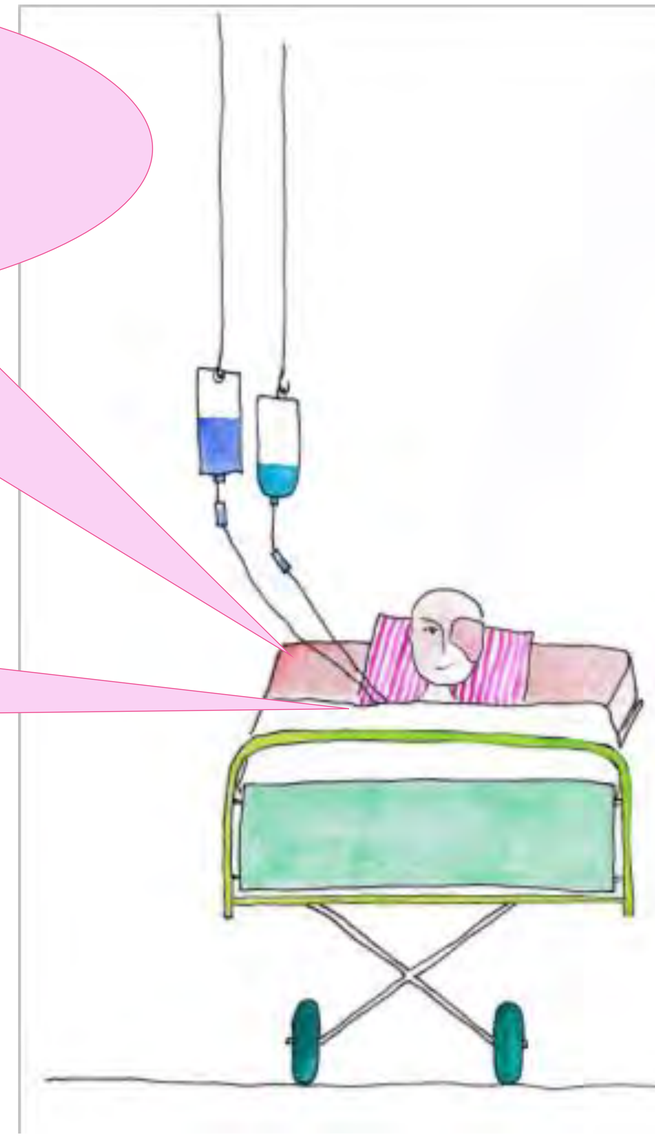
- Rare direct contacts
- Patient regularly in oncology ambulatory
- Husband: ‘she lets herself go’
  ‘it’s so much work, i cook for her and she doesn’t even touch it’
  ‘when the children come next to her bed at night, she turns away’
  ‘I feel like my wife has changed so much. I love her, but somehow she is not the woman I knew’
- Patient: ‘I’m so tired. Everything is so much work’
  ‘I’m not myself anymore’
  ‘I don’t want to die’
  ‘I don’t want to keep living this way’

Hospitalisation



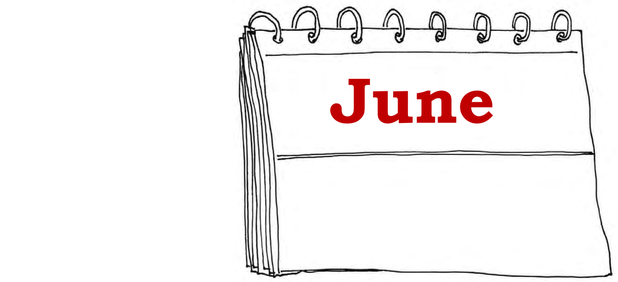
‘I don’t know if I have pain
– I’m just empty…’

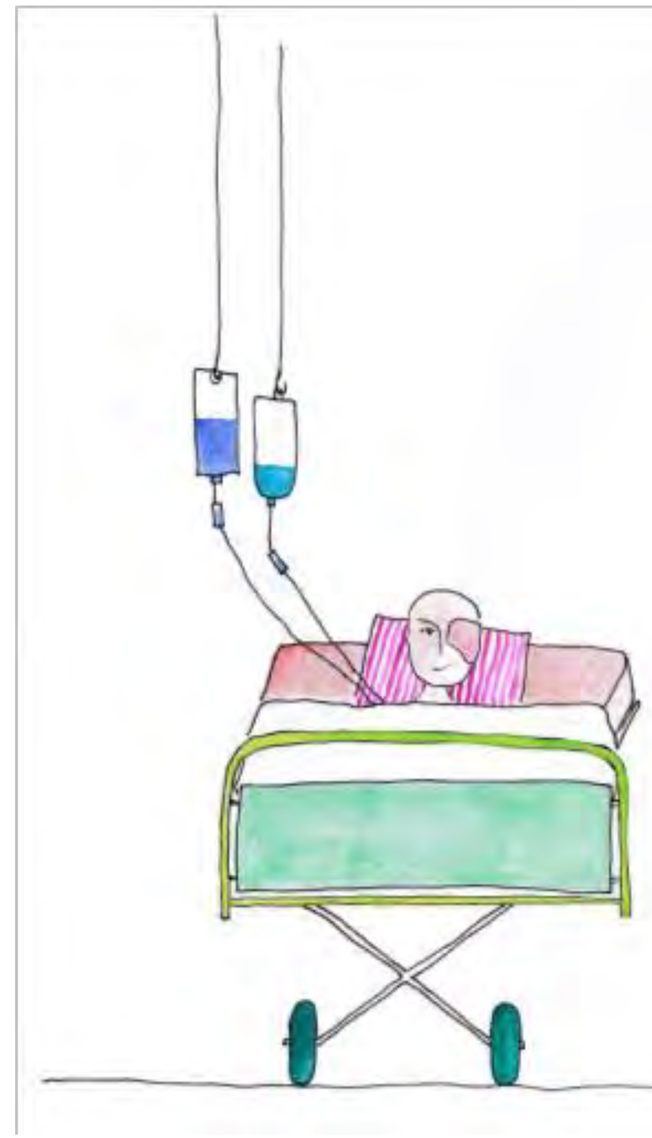
‘I’m empty.
Just empty.
I didn’t even know if I wanted to
go to hospital or not.
My husband just brought me
here. I guess it’s ok…’



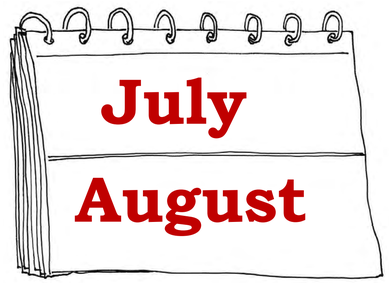
Hospitalisation

- AZ↘
- Stopp antitumor therapy
- Symptomcontrol



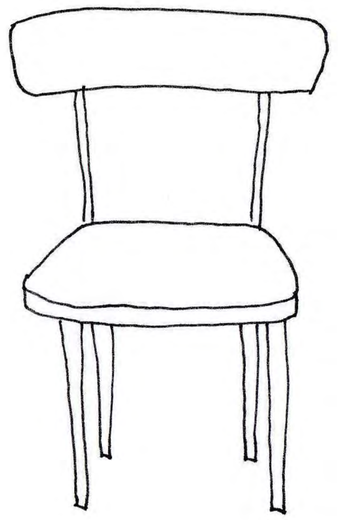


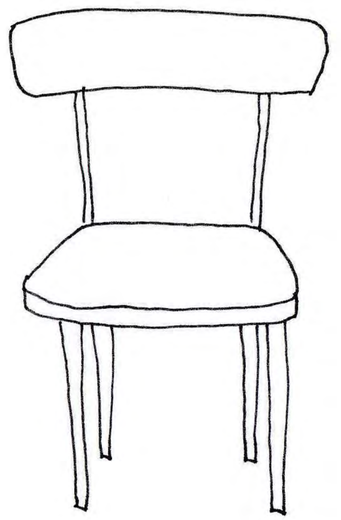
Hospitalisation



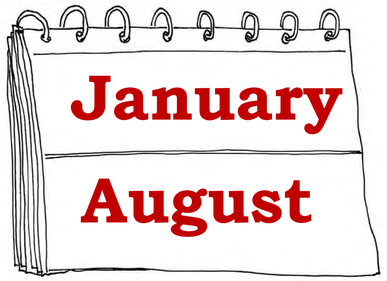
- Transfer in a Palliative Care Clinic

- Patient dies two weeks later





Mrs Monty – timeline



Unspecific symptoms

Diagnosis
and
Progression

OP

symptoms
body image

Radio

Chemo?

relaps
Metastases

OP

Chemo!

Progression

Radio

Immuno

emotional
crisis'

Progression

AZ↓

weakness
pain
breathlessness
sadness
anxiety

Palliative
Care
Unit

Stopp
tumor
therapy

death

Advance directive

vacuum

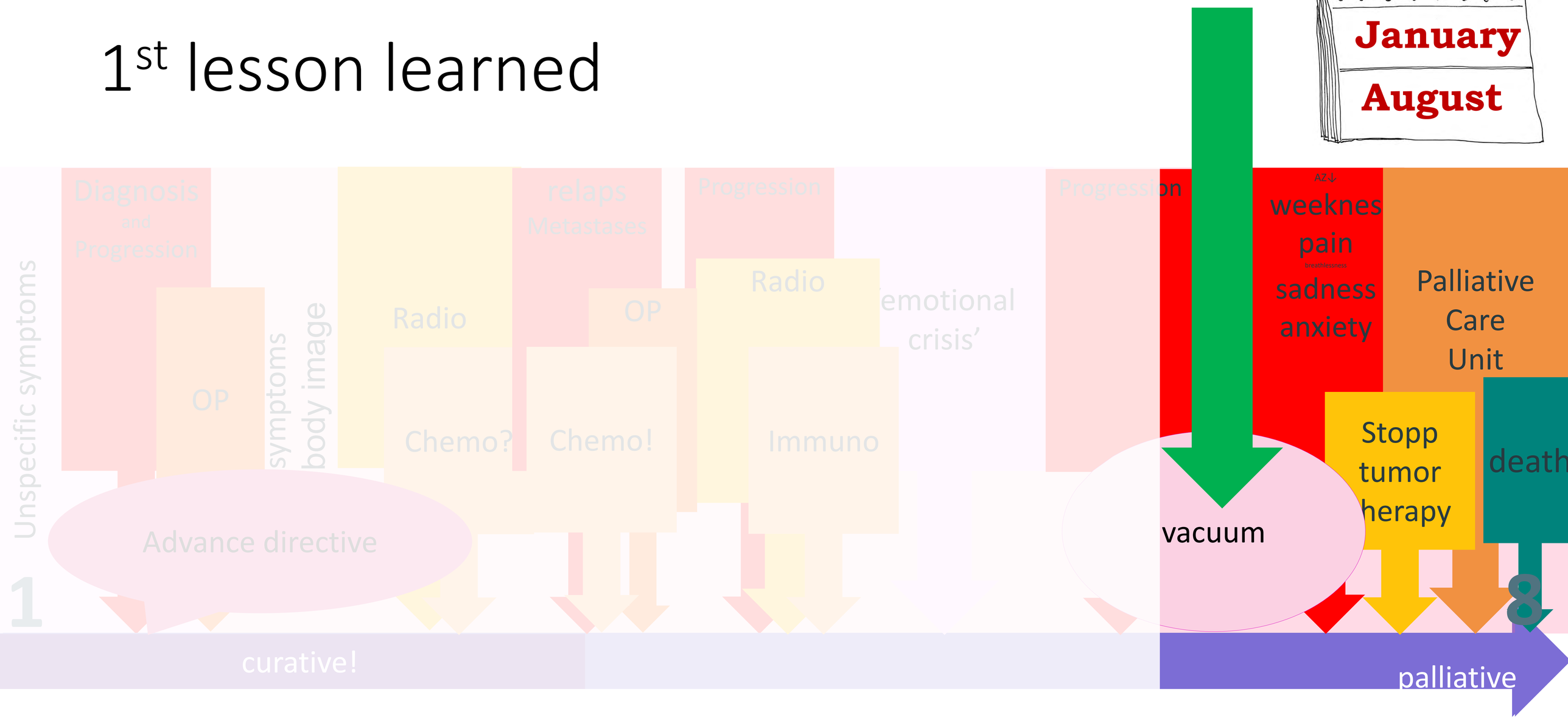
1

8

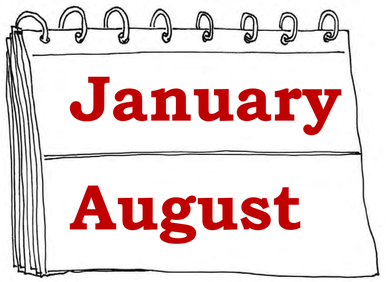
curative!

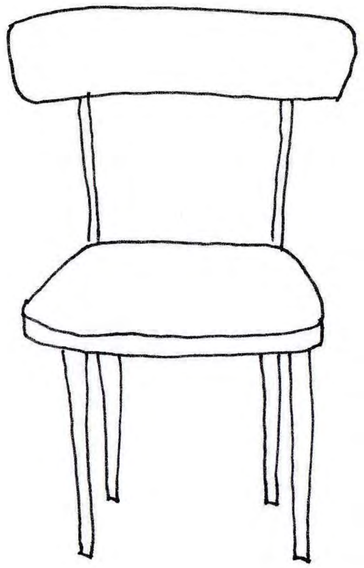
palliative

1st lesson learned



2nd lesson learned





2nd lesson learned