The Future of Palliative Oncology

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Objectives

- Communication and collusion
- Early palliative care embedded into palliative oncology
- Outcomes to palliative oncology
- Costs and incremental cost effectiveness- what is the price we are willing to pay

Trajectory of Palliative Oncology

- Existential crisis with diagnosis
- Focus on anti-cancer therapy
- Relative peace of mind on therapy with stabilization of the cancer
- Existential crisis with relapse which can be recycled with multiple lines of therapy
- Final existential crisis when transition off anti-cancer therapy

Collusion in Communication

Collusion

- “Unconscious dynamic between patient and clinician which provokes unreflective behavior, strong emotions and leads to a negative impact to care”
- “ Secret agreement”
- “ Deceitful purpose”
- “Complicit intent”

Stiefel F 2016

Collusion

- Palliation which is largely centered on tumor and tumor response and survival rather than quality of life and patient goals
- Minimalize limitations to anti-tumor therapy and toxicity
- Maintain anti-tumor therapies despite its failure as a means to maintain hope
- Individuals are taken off “ active treatment” when transitioned

Elements of Collusion

- Concealment of prognosis- bidirectional
- Hope sustained by future developments in cancer therapy
- The use of non-specific terms- “treatment”
- Promises of therapy “when you get better” despite poor performance related to cancer and its treatment
- Failure to address advanced directives and personal goals
- Application of therapies beyond the known published benefits

Collusion

- “Watchful waiting” is given little attention
- “ There is no other choice” but to continue on therapy
- Hope transformed from a verb (what do you want to accomplish with the remaining part of your life) to a noun (hope is the next treatment)

Collusion

- Collusion is fostered by medical activism- doing rather than being
- Patients know that if they take a passive approach to decision-making, the oncologist is likely elect aggressive treatment
- Accumulated information debt over time
- Patients may be relieved with the opportunity to forget what the end result is and / or plan a future which is incongruent with the course of cancer due to a lack of understanding

de Haes H 2003

The A 2001

Misdirection and Misunderstanding

- 722 patients in the CANCor survey with advanced lung cancer
- Only 1/3 recognized that therapy was unlikely to cure their cancer
- If they had knew the incurability of their cancer, they were more likely to avoid aggressive therapy at the end of life and enter a hospice program earlier

Weeks J 2012

Mack J 2015

Misdirection Both Ways

- Physician may fail to communicate goals of therapy adequately
- Patients may be unable to comprehend the fatal nature of their cancer

“ If the physician said,’ this tumor can be treated’ (meaning that treatment can prolong life), the patient heard that ‘something can be done about it’ in other words, that he or she can be cured”

The A 2000

“ When he got all the doctor said that the tumor had spread and that he would never recover or get better. But then they (he) started to talk about chemotherapy. I thought, thank goodness, he is going to get better, otherwise they wouldn’t go to all this trouble for him, would they?”

The A 2000

Clinical Outcomes to Collusion and Poor Communication

- Loss of autonomy- decisions are made without full disclosure
- Missed opportunities at the end of life
- Aggressive care at the end of life-repeated hospitalizations and deaths, ICU admissions and deaths, repeated emergency department admissions, no hospice or late hospice referral
- Complicated bereavement

“ What I find very difficult”, says Mrs. L.” is that my son cannot get over the fact that he could have spent time with his father and that the whole family could have been together (for Christmas)”

The A 2000

Ways to Avoid Collusion

- Communication training
- Early palliative care
- Consistent use of symptom and quality of life tools
- Advanced directive discussions
- Reshaping discussions away from cancer centered goals to patient-centered goals
- Mindfulness training

Early palliative care is essential to the practice of palliative oncology

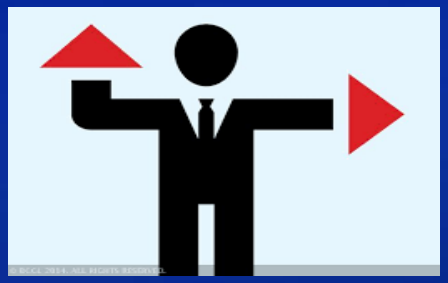
Models of Palliative Care

- Acute care model- crisis intervention in hospital late in the course of cancer
- Oncologist acts as the palliative specialist where palliative care is missing-rural setting
- “Congress model” where the oncologist utilizes multiple specialists by way of consultations-pain specialist, psychologist, chaplain, social worker
- Specialist palliative care integrated into cancer care as a standard for advanced cancer

Bruera E 2012

Models of Integration

- Prognosis- “surprise” question
- “Pathocentric”- at diagnosis of incurability
- “Oncocentric”- based on the needs and skill set of the oncologist
- Sentinel events- pathologic fracture, pleural effusion, brain metastases
- “Patient-centered”- based on symptom burden, performance score, psychosocial factors



Early palliative care

- Landmark Temel study (NEJM 2010) demonstrated improved quality of life , less depression (without antidepressants), reduced aggressive care at the end of life, and an improved 3 month survival for patients with advanced lung cancer
- Referral was based on diagnosis of incurability and not symptoms , sentinel events or transition of care
- Referral was managed by an interdisciplinary team

Important Features of Integrated Early Palliative Care

- Provide continuity- patient seen regularly
- Cooperation and collaboration between palliative specialist and oncologist
- Availability
- Embedded outpatient clinics
- Delivered on the top of “usual care”
- Competent multidisciplinary care and not single interventions (education, telephone support , supportive group therapy)

Domains of Early Palliative Care

- Expert symptom management
- Enhanced autonomy through exploring patient understanding of the goals of therapy, prognosis, preferred decision-making and advanced care planning
- Supportive through enhancement of a sense of self through coping strategies, dignity and meaning based therapy, spiritual support, family counselling and education and coordinating community support

Barriers to Integration- MASCC Survey 2015

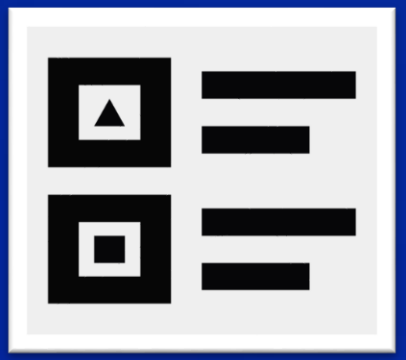
- Limited budget within the cancer center
- Funding toward drug development and anti-cancer therapies
- Limited number of trained palliative specialists
- Many cancer centers value palliative care but the willingness to fund developments is expressed in < 20% of centers

Davis M 2015

Defining Palliative Oncology: The Institute for Quality and Efficiency In Health Care (IQWIG) Report on Oncology Trials for Incurable Cancer

Gaertner J 2015

IQWIG Report



- 100 oncology studies
- 71- clear descriptions of advanced cancer
- Primary sites were mostly pancreas and lung cancer
- Prolonged survival was clearly the most important outcome
- Primary outcome was disease specific survival in 53 / 100 and progression free survival in 45 / 100, overall survival 98 / 100

IQWIG Report

- Symptom outcome as the primary outcome- 2 / 100
- Safety and study specific outcomes- 3 / 100
- Patient related outcomes (PROs) were secondary or tertiary outcomes - 36 / 100
- Appropriate PROs instruments - 21 / 100
- Term palliative care occurred i- 3 / 100 and not defined
- “Best supportive care” frequently used and poorly described

IQWIG Report

- Impact of adverse events and effects on outcomes were adequately explained - 22 / 100
- Adverse effects were poorly described as “tolerable” from the investigators point of view or minimized - 53 / 100
- Quality of life measures- 31 / 100
- Any PRO described - 40 / 100
- Harms / benefit and risks discussion - 50 / 100

Health related quality of life (QOL) is an independent prognostic factor but most instruments are physician and not patient completed measures

Colloca G 2011

Issues Measuring QOL in Palliative Cancer Trials

- Response shift
- Attrition influences QOL outcomes
- Disproportionate optimism
- Statistical but not clinically relevant changes
- QOL tools with determined meaningful clinically relevant changes used in a subgroup
- Differences in meaningful change with improved versus diminished QOL
- Missing data

Costs of Palliative Oncology

New Develops

- Imatinib 2001- beginning of targeted therapy
- Tyrosine kinase inhibitors
- Hedgehog pathway inhibitors
- Antibody targets
- Antibody- chemotherapy conjugated agents
- Anti-angiogenesis
- Histone deacetylase inhibitors
- Check point inhibitors

Cost of New Agents

- FDA Approval is based on efficacy standards- survival and toxicity
- Costs are based on what the market will bear and not either incremental value over older approved agents or recouping costs of drug development
- List price is increased each year as much as 10%.Imatinib was 30,000 USD/year 2001 and is 138, 000 USD / year 2012
- Single producers continue despite the drug being off patent

Sarpatwari A 2017

Cost of New Agents

- Targeted agents are initially used late in the course of cancer but cost effectiveness may be better with longer durations of disease control and earlier use
- Oncologists are largely unaware of the incremental cost effectiveness ratios per quality adjusted life year saved (ICER per QALYS) which leads to choices that significantly increase family financial toxicity through co-pays (and society's financial toxicity due to distribution of costs to all insured) without improving outcomes

ICER per QALYS

- Variations across geographic regions
- Usual acceptable ICER ranges between 50-100,000 USD per QALYS
- Does not play a role in approval process in the US but does in Canada (Pan-Oncology Drug Review)
- Europe registers drugs centrally, reimbursement may be determined by individual countries based on clinical and pharmacoeconomic factors

Hoch J 2013

Examples of ICER per QALYS-Biliary Tract Cancer

- Gemcitabine vs, gemcitabine plus cisplatin
- QALYS is 0.56 for gemcitabine and 0.75 for the combination
- ICER is 33,650 vs. 44,880 USD
- Sensitivity analysis : if the ICER ceiling is < 60,000 USD then gemcitabine alone is preferred and if 60,000 to 100,000 USD the drug combination is preferred
- Includes progression free survival, survival, pre and post chemotherapy health care

Roth J 2012

Second –Line Chemotherapy for Gastric Cancer

- Irinotecan- ICER QALYS < 50,000 USD
- Paclitaxel-ICER QALYS 86,800 USD
- Paclitaxel plus ramucirumab- ICER QALYS 1,056,125 USD

Lam J 2016

Surgical Resection vs Palliation of Pancreatic Cancer

- Total direct health care costs are ½ with palliation without surgery
- QALYS is 0.2 for palliation and 0.48 for resection
- ICER is 106,100 EUROS vs. 118,400 EUROS

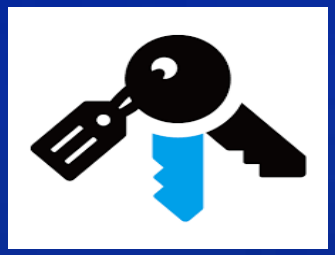
Ljungman D 2013

Molecular Targeting

Molecular Sequencing

- Defines mutations which are potential targets
- Analysis can be single genes- EGFR, ALK rearrangements (FISH, IHC staining, PCA, sequencing)
- Sequenome analysis-Next Generation Sequencing, Foundation One Sequencing Platform for multiple potential targets
- Changing face of oncology toward genomic classifications away from disease site classifications with exceptions (not all driver mutations are drivers in found in other cancer sites)

Atherly A 2012



Molecular Targeting Cost Effectiveness

- Cost of the test
- Cost of the drug targeting the mutation
- Frequency of the mutation found in the cancer population
- Effectiveness in disease control and survival
- Toxicity and the cost of managing toxicity

Molecular Targeting Cost Effectiveness

- A mutation frequency > 5% minimizes the cost factor of the assay
- Drug costs then are determined on the ICER per QALYS
- Mutation frequency < 5%: ICER per QALYS is acceptable if the cost of the assay is reduced or the population which has the mutation is enriched.
- Sequenome studies are cost effective if an actionable mutation is found in > 40% of the population
- “Negative” appeal to sequenome assays since this minimizing patient exposures to ineffective therapy. Exceptions can be PDL-1 assays for which lack of expression does not exclude responses altogether

Atherly A 2012

Cost of Palliative Care

- Cost savings to institutions particularly with bundling and value based care

Early palliative (outpatient) care

- Appointment durations-45-90 minutes
- Number of follow-ups – 4-5
- Midlevel to Physician FTE- 2 to 1 or 1 to 2
- Provider to patient ratio- 1 to 230
- Variable telephone follow-up – routine or as needed
- Cost (direct) per patient enrolled -535 USD

Gaertner J 2015

Palliative Oncology and Family Financial Toxicity

- Extension of life now with lung, colon, prostate, breast, ovarian among other primary sites
- New and accumulative toxicities over longer intervals
- In the last 12 months of life the average monthly cost is 14, 900 Canadian dollars
- Unpaid family care-giving costs accounted for 77% of total palliative costs
- The goal to stay at home means someone needs to stay with the patient
- Out of pocket expenses threaten the education, economic stability and well being of the next generation

Chai H 2014

Domains of Palliative Oncology To Be Targeted

- Communication education
- Integration of palliative care early in advanced cancer as a standard of care and quality measure
- Service structure and financial support to facilitate integration
- Incorporation of ICER per QALYS into the approval process and incorporating PROs
- Concerted effort to study and minimize family financial toxicity

Summary

- Collusion can profoundly damage patients, impair autonomy and increase the cost of care
- Integrated palliative care has both patient and medical health care benefits
- Sequenome assays are more cost effective than obtaining single gene / mutation assays depending on populations
- Drug value should move from market to ICER based on QALYS
- Family financial toxicity is a rapidly growing problem