A Review of Delirium in Oncology

CAGPO 2015

Dr. Caroline Gérin-Lajoie

Psychiatrist, Psychosocial Oncology Program,

The Ottawa Hospital Cancer Centre

Learning Objectives

- Review the diagnosis and treatment of delirium in patients with cancer
- Discuss the unique precipitating factors present in the oncology patient
- Discuss treatment options and when to refer to a psychiatrist

Conflict of Interest

- I **DO NOT** have an affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

Importance

- Frequent and often serious neurocognitive and behavioral complication in patients with cancer
- Especially advanced-stage disease, or vulnerable (elderly and dementia), but can happen anywhere in the illness trajectory
- Often under-recognized, misdiagnosed, undertreated, or inappropriately treated

Importance

- Associated with increased morbidity and mortality (independent predictor of short-term survival in advanced-stage cancer)
- Part or complete reversal can be possible depending on the nature of the precipitating factors and the goals of care
- **In advanced cancer and palliative care 50% of episodes can be reversed**

Importance

- Interferes with recognition and control of other physical and psychological sx (ex: pain)
- Impact on communication
- High distress for family and health care professionals
- Economic burden across all hospital settings (ex: increased length of hospitalization)
- Projected increase in elderly population, thus in cancer prevalence and dementia

Under recognition…Why?

- Under recognition is widely reported (nurses, physicians)
- Multiple factors ex: fluctuating nature, failure to use screening tool, hypoactive delirium, dementia, >80 y-o, visual impairment
- Differential diagnoses: depression, anxiety, akathisia, dementia
- Lack of basic knowledge re: cognitive screening, diagnosis, management, documentation often missed

Prevalence Rates

- One of the most prevalent mental disorders in general hospital practice
- 15-30% general inpatients
- 44% cancer inpatients (Pareira et al.)
- 50% of stem-cell transplant patients (JR Fann et al.)
- 85% terminal cancer patients (Massie et al.)
- 88% 6 hours before death (Lawlor et al.), last hours, days and weeks

Diagnosis

- Described for centuries, Latin: “de lira”
- Classic paper Engel and Romano 1959: global brain dysfunction
- DMS-III in 1980

- Synonyms: reversible dementia, organic brain syndrome, acute confusional state, terminal restlessness (palliative care)

Diagnostic Criteria (DSM-5), 2013

- A. Disturbance of **attention** (sustain focus and shift attention), and **awareness** (orientation)
- B. Develops over **short period** of time (hours/days), change from baseline, **fluctuates** during the day
- C. Change of **Cognition** (memory, disorientation, language, visuospatial ability or perceptual disturbance)

Diagnostic Criteria (DSM-5), 2013

- D. Not better explained by another neurocognitive disorder, not during a coma
- E. Evidence that it is a direct consequence of another medical condition or substances (intox, w/d) or toxin or multiple etiologies
- *Gold- standard criteria in most studies

Other Clinical Features

- Prodromal sx: restlessness, anxiety, irritability, sleep disturbance
- Increased or decreased psychomotor activity
- Disturbance of sleep-wake cycle
- Mood sx (depression to euphoria)
- Disorganized thought process
- Incoherent speech
- Neurological findings (asterixis, myoclonus, tremor, frontal release signs, muscle tone)
- EEG: diffuse global slowing is a classic finding

Delirium Subtypes

- Based on **psychomotor behavior** and level of **arousal**
- **Hyperactive** (hyperalert): restlessness, agitation, hypervigilance, hallucinations, delusions, disorientation
- **Hypoactive** (hypoalert or hypoaroused): psychomotor retardation, lethargy, reduced awareness, confusion
- **Mixed**- alternating features

Delirium Subtypes

May have different causes, prognoses and treatment responses

- **Hypoactive**: due to hypoxia, dehydration, metabolic disturbances or hepatic encephalopathy, higher mortality risk, more resistant to pharmacology treatment

- **Hyperactive**: alcohol and drug withdrawal, drug intoxication, medication adverse effects

Experiential Impact of Delirium For Patients

- Study: >50% recalled delirium, of which 80% reported severe distress (Breitbart et al.)
- Study: 74% recall rate, of which 81% reported distress (Bruera et al.)
- Both found recall similar in subtypes (hypo, hyperactive)
- Almost 30% recalled, of which 73% severe or very severe distress (Grover et al., more recent)

Experiential Impact of Delirium For Patients

- Anxious
- Threatened
- Fearful
- Visual hallucinations
- Clouding
- Being an outsider
- Difficulty communicating
- Not understand what staff wanted
- Misperceptions, hallucinations, delusions often of staff, patients, deceased family members
- Loss of control
- May be reluctant to discuss afterwards

Experiential Impact of Delirium For Families

- Distressing to witness (agitation/hallucinations)
- Especially when Hyperactive agitated type
- Concerns about the importance of delirium
- Caregivers: anxiety, stress, exhaustion, guilt
- Important role in the early detection (prodrome)

Experiential Impact of Delirium For the Health Care Providers

- Nursing care: challenging, stressful, night time
- Difficulty establishing contact and understanding the patients' experiences
- Increased stress and strain (>Hyperactive type)
- Vulnerability, frustration
- Need for education/training/strategies to support staff, early recognition, collaborative team approach
- Rewarding when patients settle

Assessment Tools (appropriate in cancer or palliative care settings)

- Screening
- Diagnosis
- Severity-Monitoring

Assessment tools for Screening

- MMSE
- SOMCT
- CAM*
- MDAS
- NuDESC
- DOSS
- SQiD

Assessment tools for Diagnosis

- DSM-5
- ICD-10

Assessment Tools for Severity Rating

- MDAS*
- DRS-R-98*
- DOM
- NuDESC
- DOSS

Pathophysiology

- **Underlying mechanism is complex, dysfunction of multiple regions of the brain**

- Neuroinflammatory hypothesis
- Neuronal aging hypothesis
- Oxidative stress hypothesis
- Neurotransmitter hypothesis

- Most often in the terminally ill the etiology is multifactorial or may not be determined (<50%)

Pathophysiology

- Dysregulation of neurotransmitters is a potential mechanism underlying the pathophysiology

- Final common pathway to different specific etiologies of delirium: dopamine, acetylcholine or second messenger system, in prefrontal cortex, posterior parietal cortex, antero-medial thalamus

Conceptual Framework: Inouye's predictive model of delirium

- Widely accepted
- Relationship between baseline vulnerability (**Predisposing Factors**) and superimposed factors (**Precipitating Factors**) interact in a reciprocal fashion

Predisposing Risk Factors

Non-cancer intracranial

- Dementia
- Older age
- Depression
- Hx of alcohol abuse
- Hx of CVD
- Previous delirium

Cancer-related intracranial

- Primary brain neoplasms
- Brain or leptomeningeal mets
- Cognitive impairment after chemo?
- Cognitive deficits after rad?

Predisposing Risk Factors

Systemic vulnerability factors

- Anorexia-cachexia?
- Frailty?
- Hypoalbuminemia
- Chronic cancer-related inflammation
- Reduced functional performance status
- Organ dysfunction related to cancer
- Illness severity

Miscellaneous

- Visual impairment
- Hearing impairment
- Sleep apnea
- Polypharmacy
- Low educational attainment or cognitive reserve

Precipitating Factors in Cancer

Intracranial

- Primary brain Ca
- Brain or leptomeningeal mets
- Paraneoplastic encephalitis
- Post-ictal phase
- Nonconvulsive status epilepticus
- Reversible posterior leukoencephalopathy syndrome (RPLS)
- Cerebral edema after brain rad
- CVA

Medications

- Opiods*
- Benzodiazepines*
- Antidepressants
- Antihistamines
- Anticholinergics?*
- Cytotoxic chemo
- Corticosteroids*
- Quinolones

Precipitating Factors in Cancer

Metabolic/electrolyte

- Na abnormalities
- Dehydration/hypyvolemia
- Mg abnormalities
- Hypercalcemia
- Acidosis, hypoxia
- Thiamine deficiency

Others

- Medication withdrawal
- Infection/sepsis
- Organ dysfunction/failure
- Endocrine
- Hematologic (anemia, DIC)
- Surgery
- Uncontrolled pain
- Room changes

Management Strategies (Clinical Pathway)

- Regular delirium screening
- Preventive approach (high risk): minimize psychotropic meds, hydrate
- Confirm diagnosis: tools/DSM-5
- Education & support for families: reassure/review goals of care

Management Strategies (Clinical Pathway)

- Monitor delirium severity: tools

- Symptomatic management for all patients: Pharmaco and Nonpharmacological treatment

AND

- Identify and treat reversible precipitants: investigations, hydration, antibiotics…

Potential Outcomes

- 1. **Resolution of delirium**: awake, alert, calm, comfortable, cognitively intact, not psychotic, communicating coherently (taper antipsychotics, screen for further episodes)
- 2. **Refractory delirium at the end of life** (involve palliative care, consider palliative sedation)
- 3. **Persistent delirium or partial resolution** (R/O underlying dementia, maintain antipsychotics, monitor severity)

Nonpharmacological Prevention

- Needs further research
- NICE guidelines recommend several preventive interventions
- Ex: Targets 6 risk factors: cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment and dehydration in hospitalized older patients

Pharmacological Prevention

- Used in ICU and post op patients
- ?Prophyactic melatonin?
- Needs further research
- No medication with FDA approval for treatment or prevention of delirium to date

Reversing Delirium

- Hinges on the identification and treatment of precipitant factors, and goals of care
- Average of 3 (1-6) precipitating factors
- Detailed history from family and staff of baseline mental status
- Verify the current fluctuating mental status (nurses notes)

Reversing Delirium

- Ask about alcohol or substances
- Medication review: opioid-induced neurotoxicity (OIN), benzodiazepines, steroids, antidepressants (taper if possible)
- Physical Exam
- Investigations: Labs, EEG, CT, LP (See Precipitants)

Symptomatic Management Nonpharmacological

- Supported by current guidelines
- Beneficial for cancer patients at risk for delirium
- No know risks associated

Nonpharmacology Intervention

- Safe environment
- Minimize noise, avoid excess light or darkness
- Educating family and staff
- Normalization of sleep
- Promotion of safe mobility
- Monitoring for dehydration/electrolyte abn.
- Monitoring nutrition
- Monitoring sensory deficits (visual and hearing aids)
- Monitoring bowel and bladder functioning
- Orientation board, clock, familiar objects
- Encouraging cognitively stimulating activities

Symptomatic Management Pharmacological

- Often necessary
- **Short term, low-dose antipsychotics is supported, with close monitoring** (for agitation and perceptual disturbances)
- Low dose **Haldol** remains the standard (despite limited evidence)
- Related to selective D2-receptor antagonism (anti-dopaminergic effect, non sedating, few anticholinergic side effects)

Symptomatic Management Pharmacological

- Growing evidence for atypical antipsychotics
- Less affinity for D2 receptor, high degree of 5-HT serotonin receptor occupancy = more sedating and less EPS
- Olanzapine, risperidone, quetiapine
- If EPS or contraindication for typicals
- Associated with weight gain and metabolic syndrome (less significant if short-term)

Symptomatic Management Pharmacological

- Data: antipsychotics are effective in improving or resolving delirium in the medically ill and in those with cancer
- 1/3 experienced benefit at 48 hours
- Perceptual disturbances and delusions can occur more frequently in hypoactive delirium then previously reported

Antipsychotics considerations

- Risk of EPS (triad bradykinesia, tremor, rigidity)
- Sedation
- Anticholinergic adverse effects
- Cardiac arrhythmias: FDA warning of QTc prolongation and Torsades de Pointes with IV Haldol
- Possible drug-drug interactions
- Neuroleptic Malignant Syndrome: rare, mostly reported in parenteral haldol, can occur in atypicals (catatonia, rigidity, hyperpyrexia)

Antipsychotic doses

- Haldol:
  - 0.5-2mg q2-12 h (average 2-10mg/day, most need under 20mg/day)
  - PO, IV, IM, SC
  - Parenteral dosing twice as potent
  - ECG for QTc interval, especially if parenteral
  - May add Lorazepam 0.5-1mg q2-4h for agitation

Antipsychotic Doses

- Olanzapine:
  - 2.5-5mg PO and dissolving, q12-24h (5-12mg/day in terminal patients)
  - Sedation
  - Poor response in older age, dementia, hypoactive subtype

Antipsychotic Doses

- Risperidone:
  - 0.25-1mg q12-24h
  - EPS, orthostatic hypotension
- Quetipine
  - 12.5-100mg q12-24h
  - Sedation
  - Orthostatic hypotension

Symptomatic Management Pharmacological: other meds

- GABA agonists: Lorazepam used for alcohol withdrawal, Midazolam (palliative care sedation)

- Psychostimulents in hypoactive delirium: not currently recommended, limited evidence
- **Cholinersterase inhibitors**: Donepezil, Rivastigmine, not recommended, no evidence
- **Alpha-2 (NE) receptor agonist**: IV Dexmedetomidine (ICU), no evidence for use in cancer

Refractory Delirium

When all attempts to control its sx have failed, and when there is a lack of other methods for palliation within an acceptable time frame and without unacceptable adverse effects"

- Common indication for palliative sedation
- Others: refractory dyspnea, respiratory distress, seizures, terminal hemorrhage, rarely intractable pain

Palliative Sedation

The monitored use of proportionate sedative medication to reduce patient's awareness of intractable and refractory sx near the end of life (last days to weeks)

- Refractory agitated delirium is most common cause
- Does not shorten life, ethically accepted
- Midazolam is most frequently used (rapid onset, short half-life, dose dependent sedative effect)

- Others: lorazepam, methotrimeprazine, chlorpromazine, phenobarbitol, dexmedetomidine, propofol infusion
- Consult Palliative Care Specialists

Key Points

- Frequent neurocognitive complication in patients with cancer
- Especially advanced-stage disease, or vulnerable (elderly and dementia)
- Often under-recognized or misdiagnosed
- Impact on communication: distress for family and HCPs
- Interferes with control of other sx (ex: pain)

Key Points

- Associated with increased morbidity
- Investigations and treatment depend on goals of care and prognosis
- Part or complete reversal can be possible depending on the nature of the precipitating factors an goals of care
- Pharmacologic treatment is indicated for most
- Antipsychotics are the drug of choice

References

- Delirium in patients with cancer: assessment, impact, mechanisms and management, PG Lawlor & SH Bush, 2015
- Evidence-Based Treatment of Delirium in Patients with Cancer, W Breitbard & Y Alici, 2012
- The Assessment and Management of Delirium in Cancer Patients, SH Bush & E Bruera, 2009
- Delirium in advanced cancer patients, C Centeno et al, 2004

The Management of Depression in Patients with Cancer CAGPO 2015

Dr. Caroline Gérin-Lajoie

Psychiatrist, Psychosocial Oncology Program, The Ottawa Hospital Cancer Centre

Learning Objectives

- Review the diagnosis and treatment of depression in patients with cancer
- Discuss the unique precipitating factors present in the oncology patient
- Discuss treatment options and when to refer to a psychiatrist

Conflict of Interest

- I **DO NOT** have an affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

All health professionals who work with patients/families affected by cancer need to be aware of the prevalence, impact, and need to respond to the “continuum of distress”… from mild to severe distress, up to psychiatric symptoms or disorder

Cancer Trajectory

- Also referred to as the cancer experience, continuum, journey
- Each phase has its unique set of stresses and challenges
- Normalization and education can be very helpful

Key Points in The Cancer Trajectory

- Diagnosis
- Acute Treatment
- Remission
- Follow-up
- Relapse
- “Chronic illness” or “survivorship”
- Palliation

DISTRESS

- Cancer-related distress: “ psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment” (NCCN Guidelines)

- Prevalence: 28-87%

Prevalence of Depression in Cancer

- Clinical rule of thumb: 25% of cancer patients are likely to be depressed enough at some point in the course of disease to warrant evaluation and treatment
- Advanced cancer median prevalence: 15%, “global suffering”, “total pain”

Research in Cancer Patients

- Absence of strong cancer-specific evidence, insufficient new evidence in the last decade
- Evidence is extrapolated from primary psychiatric and other medical populations
- Based on NICE clinical guidelines and Depression in Adults with a Chronic Physical Health Problem

Other Guidelines

- Canadian Association of Psychosocial Oncology's depression symptoms management guideline (SMG)

- A Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer

Cancer Care Ontario
Guideline #19-4

Program in Evidence-Based Care (PEBC)
"The Management of Depression in Patients with Cancer"

Report Date: May 11, 2015

Target Population

- Adult patients with cancer, diagnosed with a major depressive disorder based on a structured diagnostic interview or suspected depressive disorder based on meeting a threshold on a validated rating scale

- To be used by multidisciplinary health care providers

Guideline also includes

- Quick reference guide for the initial management of depression
- Delivery of intervention according to the stepped care model
- Practical tools (screening scales, diagnostic criteria, psychological interventions, antidepressant prescribing)

8 Recommendations

1. Screening of patients
2. General management principles
3. Pharmacological or psychological/psychosocial interventions
4. Depression severity and a stepped care approach
5. Collaborative care interventions
6. Specialist referral
7. Selection of psychological therapies
8. Use of antidepressant medication

Depression Management Algorithm

- Establish the presence of a Depressive Disorder
- Rule out other Medial Condition (TSH, B12, folate, anemia,…)
- Assess suicidal ideation, plan, intent
- Optimize treatment of cancer-related physical symptoms
- Validated Rating Scale to assess severity and monitor response to treatment
- Deliver intervention with intensity corresponding to Depression Severity (Stepped Care Model)

R1: Screening of patients with cancer for distress and depression

- Patients with cancer should be screened
- Screening for Distress, the 6th Vital Sign, is a standard of care in multiple cancer care guidelines
- ESAS in Canada the most commonly used for various symptoms

Select Validated Depression Screening Scales

- Hamilton Rating Scale for Depression (HRSD)
- Centre for Epidemiologic Studies Depression Scale (CES-D)
- *Patient Health Questionnaire 9 (PHQ-9)
- Hospital Anxiety and Depression Scale (HADS)
- Beck Depression Inventory II (BDI-II)

DSM-5 Criteria for Major Depression

- Is the standard for diagnosing Major Depression in people with cancer
- 5 or more sx, for at least 2 weeks duration, change from previous functioning, and including at least one: either depressed mood, or loss of interest/ pleasure
- NOTE: do not include sx attributable to another medical condition

DSM-5 Criteria for Major Depression

- Symptoms: “SIG E CAPS”

- Depressed mood
- Diminished interest or pleasure
- Significant weight loss
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive or inappropriate guilt
- Diminished concentration or indecisiveness
- Suicidal ideation

DSM-5 Criteria for Major Depression

- Clinically significant distress/impairment of functioning
- Not secondary to substances or general medical condition
- Not bereavement

Diagnosis of Depression in Cancer

- <u>May rest upon affective and cognitive sx:</u>

- Depressed mood, anhedonia, loss of interest/apathy, poor concentration or memory, slowed sluggish thoughts, pessimism/negativity, worthlessness, excessive **guilt**, **helplessness**, **hopelessness**, **suicidal ideation**

Depression Severity Criteria

- **Subthreshold** depressive sx: <5 sx of depression

- **Mild** depression: few sx over the minimum required to make a dx, minor impairment on functioning
- **Severe** depression: many sx and markedly interfere with functioning
- **Moderate**: in between mild and severe

Medical Causes of Depression

- CNS: Parkinson's, CVA, tumors
- Aids
- Hypokalemia
- Hypo/Hyperthyroidism
- Pancreatic CA
- Hepatitis, Cirrhosis
- Mononucleosis
- Occult malignancy
- Anemia
- Cushing's (hypercortisolism)

Cancer Illness and Treatment-related Factors

- Tumors or metastases to CNS
- Metabolic complications (hypercalcemia)
- Tumor-related toxins
- Autoimmune reactions
- Viral infections
- Nutritional deficiencies (B12, Folate)
- Radiation to brain or head and neck

Pharmacological Causes of Depression

- Cardiac and antihypertensives
- Sedatives and hypnotics
- Steroids and hormones
- Stimulants and appetite suppressants
- Psychotropic drugs (benzo)
- Neurological agents
- Analgesics/anti-inflammatory
- Antibacterial and antifungal
- NSAIDs
- Anticholinesterases
- Antineoplastic (vincristine, vinblastine, asparaginase, intrathecal methotrexate, interferon, interleukin, tamoxifen)

R2: General management principles

- Provide psychoeducation about depression in patients with cancer (NCI handouts)
- Inform patients about the impact of depression on cancer outcomes
- Destigmatize clinical depression
- Investigate medical contributors to depression (TSH, B12, folate,…)

R2: General management principles

- Assess and optimize cancer-related physical symptom control
- Involve and educate family members
- Discuss treatment options
- Consider a validated depression rating scale to monitor over time

R3: Pharmacological or psychological/psychosocial interventions

- Patients with cancer and a diagnosed major depression may benefit from pharmacological or psychosocial interventions either alone or in combination
- Effectiveness for psychosocial and pharmacological interventions for moderate depression is equal
- Pharmacological treatment most effective in more severe depression
- Combined psychosocial and pharmacologic interventions should be considered for severe depression

R4: Depression severity and stepped care approach

- Provision of support and psychoeducation for all patients
- Assessment of severity of depression for each patient
- **Low-intensity interventions** for mild-moderate depression or persistent subthreshold
- **High-intensity interventions** for non-responsive or moderate-severe depression

R4: Depression severity and stepped care approach

Low-intensity psychosocial intervention

- Group physical activity programs
- Group-based peer support or self-help programs
- Guided self-help programs (CBT based)
- Behavioural activation
- Problem solving

High-intensity psychosocial intervention

- Individual or group CBT
- Behavioural couples' therapy
- Individual or group supportive-expressive psychotherapies

R5: Collaborative care interventions

- Active collaboration between oncologist or primary care provider and a patient care manager (nurse, SW, psychologist) with pharmacological treatment supervised by a consulting psychiatrist as needed

- Multi-component interventions, at a range of intensity levels, depending on local resources
- Typically include measurement-based care
- Follows principles of stepped care

R5: Collaborative care interventions

- Meta-analysis of collaborative care interventions in patients with moderate to severe major depression and cancer

- Significantly more likely to experience 50% reduction of score on rating scale, lower mean scores, remission more likely

R6: Specialist referral

- Risk of harm
- Complex psychosocial cases
- Patients experience persistent symptoms after initial intervention or severe depression
- Diagnosis is unclear
- Delivery of specific psychotherapies requiring specialized training

R7: Selection of psychological therapies

- Insufficient evidence for superiority of one modality over another
- Selection based on patient factors and local resource availability
- Considered first for mild to moderate depression (most cancer patients)
- Non-mental health specialists can be trained in basic psychosocial interventions

R7: Selection of psychological therapies

Trained health-care professionals

- Empathic communication (PEBC Guideline 19-2 on Provider-patient communication)
- Psychoeducation (National Cancer Institute handouts)
- Problem solving
- Behavioural activation

Specially trained therapists

- Individual or group CBT
- Behavioural couples' therapy
- Individual or group supportive-expressive psychotherapies

Psychological interventions used for depression in cancer

- Group-based peer support (self-help) programs
- Structured group physical activity programs
- Mindfulness Based Stress Reduction and Mindfulness Based Cognitive Therapy
- Cognitive Behavioural Therapy
- Behavioural activation therapy
- Problem solving therapy
- Interpersonal therapy
- Behavioural couples' therapy
- Supportive-expressive therapy
- Core conflictual relationship theme
- Dignity therapy
- Meaning-Centred psychotherapy
- Managing Cancer and Living Meaningfully (CALM)

R8: Use of antidepressant medication

- Do not use it routinely for subthreshold depressive symptoms or mild depression (higher risk:benefit ratio)
- Considered first for severe depression
- SSRI's (citalopram, escitalopram) should be first resort due to best tolerability and least potential for drug interactions
- Roles also for anxiety, hot flashes, sleep disturbances, appetite enhancement, neuropathic pain, nausea

Standard first-line antidepressants for patients with cancer

- **Citalopram/Escitalopram**
  - Start: 10-20 mg daily/ 5-10 mg qHS
  - Goal: 20-40 mg daily/ 10-20 mg qHS
  - Max: 40 mg daily/ 20 mg qHS
- Escitalopram may have more rapid onset than other SSRIs (1-3 weeks)

- **Venlafaxine/Desvenlafaxine**
  - Start: 37.5-75mg qAM/50mg qAM
  - Goal: 75-225mg qAM/50-100mg qAM
  - Max: 300mg qAM/100mg qAM
  - Optimal for tamoxifen, consider when hot flashes

Standard first-line antidepressants for patients with cancer

- **Mirtazapine**
  - Start: 7.5-15mg qHS
  - Goal: 15-45mg qH
  - Max: 60mg qHS
- Consider for insomnia, anorexia, nausea, rapid dissolve formulation

- **Duloxetine**
  - Start: 30mg qAM
  - Goal: 30-60 mgqAM
  - Max: 120mg qAM
- Separate indication for neuropathic pain and chronic pain

Standard first-line antidepressants for patients with cancer

- Buproprion XL
  - Start: 150mg qAM
  - Goal: 150-300mg qAM
  - Max: 450mg qAM

- Consider for prominent fatigue, aids sexual function, smoking cessation aid, weight neutral

Practical tools: Selecting an Antidepressant

- Past psychiatric history (positive response)
- Family psychiatric history (positive response)
- Concurrent medication (drug interactions)
- Somatic symptoms profile (sedation, weight gain)
- Potential dual benefit (neuropathic pain, hot flashes)
- Type of cancer (avoid bupropion in CNS)
- Comorbidities (avoid TCA's in cardiac disease)
- Cancer prognosis (consider psychostimulants if very short life expectancy)

Practical tools: Initiating an Antidepressant

- Screen for medical contributors and substance use (TSH, vitamin B12, folate…)
- Start at lowest dose (avoid side effects)
- Discuss that side effects should resolve within a week
- Therapeutic benefit can take 4 to 6 weeks to reach full effect
- Need to take medications daily and even after remission
- Counsel about potential discontinuation symptoms if stopped abruptly
- Reassure that dependence and tolerance does not occur
- Discuss concerns related to antidepressants and potential increased suicidality

Practical tools: Maintaining an Antidepressant

- Follow every 2 to 4 weeks until remission
- Assess response after 3 to 4 weeks at therapeutic dose, increase dose if no response
- Switch medication if no response after 6 weeks
- Continue at effective dose for at least 6 months after full remission
- If history of recurrent depression should continue at least 2 years or indefinitely

Practical tools: Maintaining an Antidepressant

- Discontinuation syndromes (malaise, dizziness, agitation, headache, nausea) may occur with abrupt termination or missed doses at high dosage levels
- Discontinuation syndromes more common with antidepressants that have a short half-life (venlafaxine, paroxetine)
- Taper over 4 weeks, symptoms may be more prominent toward the end of the taper
- Symptoms self-limiting over 1 week

R8: Use of antidepressant medication

- Concerns about interactions between **Tamoxifen and antidepressants** that inhibit cytochrome P450 2D6 (CYP2D6)
- Meta-analyses suggest this does not translate into increased breast cancer recurrent rates or mortality rates
- Existing recommendations still caution avoidance of potent CYP2D6 inhibitors (paroxetine, fluoxetine, high-dose sertraline, buproprion)
- Prefer low CYP2D6 inhibition: citalopram/escitalopram, venlafaxine/desvenlafaxine, mirtazapine) as first-line agents