Buprenorphine for the Treatment of Pain in Cancer Patients

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Disclosures

- Marcin Chwistek has no disclosures.
- Dylan Sherry has no disclosures.
- Leigh Kinczewski has no disclosures.

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Learning Objectives

1. Discuss how buprenorphine can be a preferred opioid analgesic for cancer patients.
2. Identify challenges when using buprenorphine for cancer patients.
3. Review our clinical experience and research findings using buprenorphine for cancer pain.
4. Consider future directions for buprenorphine research and use in cancer patients.

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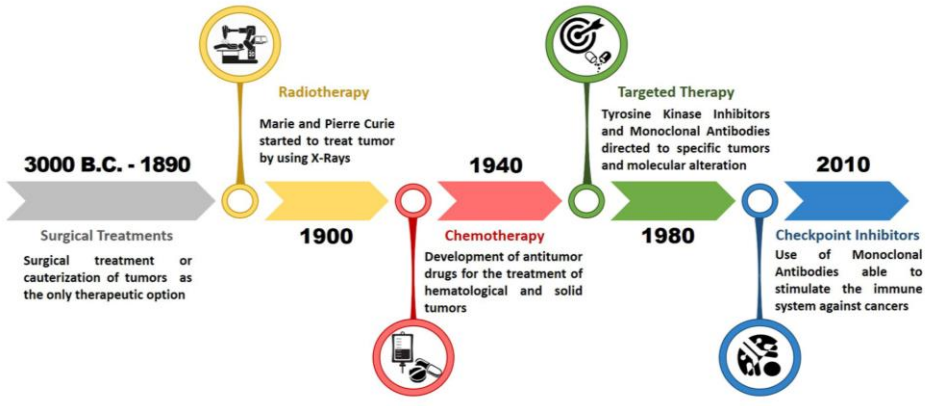
Changing Landscape in Oncology



1. Falzone L, Salomone S, Libra M. Evolution of cancer pharmacological treatments at the turn of the third millennium. *Front Pharmacol*. 2018;9:1300. doi:10.3389/fphar.2018.01300

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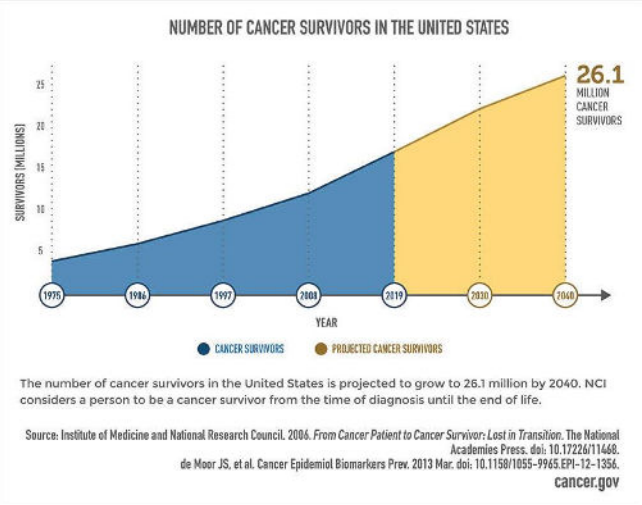
Cancer as a Chronic Condition



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Treating Cancer-Related Pain

- Opioids remain the mainstay in treating cancer-related pain (3,4)
- Long Term Opioid Therapy comes with challenges (5)
  - Hormonal Dysregulation
  - Cognitive Impairment
  - Depression
  - Non-Medical Opioid Use

3. Wiffen, P. J.; Wee, B.; Derry, S.; Bell, R. F.; Moore, R. A. Opioids for Cancer Pain - an Overview of Cochrane Reviews. Cochrane Database Syst. Rev. 2017, 7 (7), CD012592.
4. Caraceni, A.; Hanks, G.; Kaasa, S.; Bennett, M. I.; Brunelli, C.; Cherny, N.; Dale, O.; De Conno, F.; Fallon, M.; Hanna, M.; Haugen, D. F.; Juhl, G.; King, S.; Klepstad, P.; Laugsand, E. A.; Maltoni, M.; Mercadante, S.; Nabal, M.; Pigni, A.; Radbruch, L.; Reid, C.; Sjogren, P.; Stone, P. C.; Tassinari, D.; Zeppetella, G.; European Palliative Care Research Collaborative (EPCRC); European Association for Palliative Care (EAPC). Use of Opioid Analgesics in the Treatment of Cancer Pain: Evidence-Based Recommendations from the EAPC. Lancet Oncol. 2012, 13 (2), e58-68.
5. Manhapra, A. Complex Persistent Opioid Dependence—an Opioid-Induced Chronic Pain Syndrome. Curr. Treat. Options Oncol. 2022, 23 (7), 921–935

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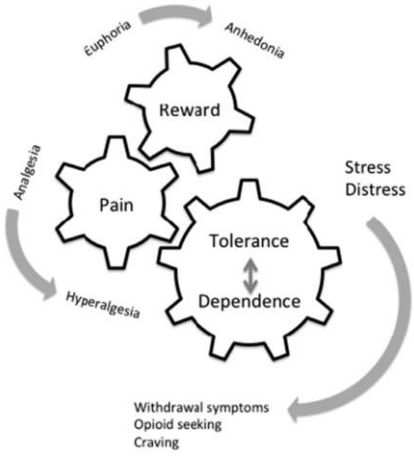
Complex Persistent Opioid Dependence



6. Ballantyne JC. Opioids for the treatment of chronic pain: mistakes made, lessons learned, and future directions. *Anesth Analg*. 2017;125(5):1769-1778. doi:10.1213/ANE.0000000000002500

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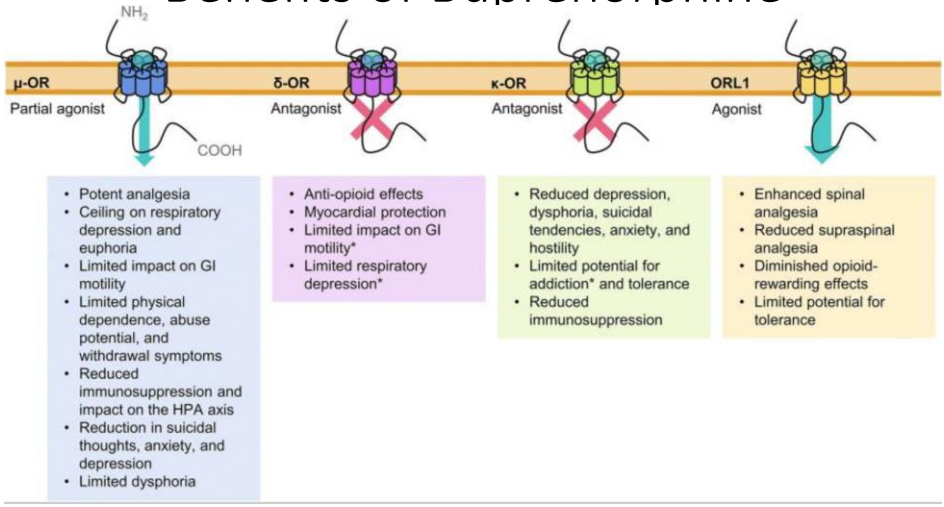
Benefits of Buprenorphine



7. Gudin J, Fudin J. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain. Pain Ther. 2020 Jun;9(1):41-54. doi: 10.1007/s40122-019-00143-6. Epub 2020 Jan 28. PMID: 31994020; PMCID: PMC7203271.

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Side Effect Profile

Full Agonist Opioids (Morphine, Oxycodone, Hydromorphone)

- Constipation!
- Cognitive Impairment
- Tolerance
- Withdrawal Symptoms
- Long Term Side Effects

Buprenorphine (Suboxone, Belbuca, Butrans)

- 1-5% in studies
- Driving w/ methadone vs. bupe
- ORL1 blocks tolerance
- Better than clonidine
- Not immunosuppressive and does not affect HPA axis

8. Davis MP. Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain. J Support Oncol. 2012 Nov-Dec;10(6):209-19. doi: 10.1016/j.suponc.2012.05.002. Epub 2012 Jul 17. PMID: 22809652.

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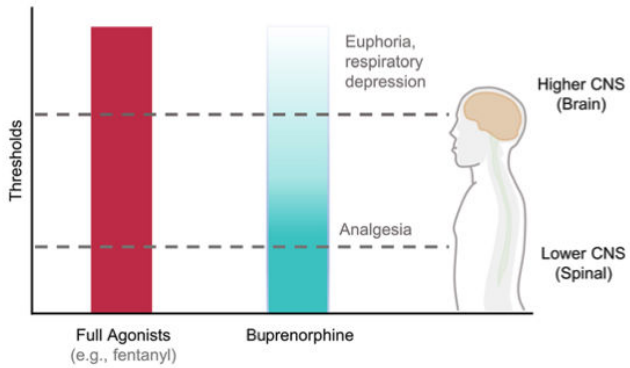
Buprenorphine activity provides analgesia while limiting euphoria and respiratory depression.



9. Miller, J. C., Brooks, M. A., Wurzel, K. E., Cox, E. J., & Wurzel, J. F. (2023). A guide to expanding the use of buprenorphine beyond standard initiations for opioid use disorder. *Drugs in R&D*.

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Study	Design	Significant Findings
Pace, et al. (2007) *Buprenorphine in Long-Term Control of Chronic Pain in Cancer Patients.*	Randomized, 2 arm, open label	Patients (n=52) on BTS had better pain control with fewer side effects compared to Morphine ER.
Wolff, et al. (2012) *Systematic Review of Efficacy and Safety of Buprenorphine Versus Fentanyl or Morphine in Patients with Chronic Moderate to Severe Pain*	Systematic review	Indirect comparison of 8 studies – higher rates of discontinuation due to AE in Fentanyl than BTS. No significant difference in pain or treatment discontinuation due to lack of effect between two groups.
Corli, et al. (2016) *Are Strong Opioids Equally Effective and Safe in the Treatment of Chronic Cancer Pain? A Multicenter Randomized Phase IV 'Real Life' Trial on the Variability of Response to Opioids.*	RCT, 4 arm, open label	Patients (n=520) randomized to Oxycodone ER, Morphine ER, Fentanyl TD, BTS. All patients with improved pain. Morphine required the most rotations and had most neurotoxicity.
Mellili, et al. (2014) *Transdermal Opioids for Cancer Pain Control in Patients with Renal Impairment.*	Parallel active control	Patients (n=44) with renal impairment received BTS patients without renal impairment Fentanyl TD. BTS patients had similar pain control and frequency of AE.

10. Pace, M. C., Passavanti, M. B., Grella, et al. (2007). Buprenorphine in long-term control of chronic pain in cancer patients. Frontiers in Bioscience, 12, 1291–1299.
11. Wolff, R. F., Aune, D., Truyers, C., et al (2012). Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. Current Medical Research and Opinion, 28(5), 833–845.
12. Corli, O., Floriani, I., Roberto, A., et al. (2016). Are strong opioids equally effective and safe in the treatment of chronic cancer pain? A multicenter randomized phase IV "real life" trial on the variability of response to opioids. Annals of Oncology, 27(6), 1107–1115.
13. Melilli G, Samolsky Dekel BG, Frenquelli C, et al. Transdermal opioids for cancer pain control in patients with renal impairment. J Opioid Manag. 2014;10(2):85-93.

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How We Use Buprenorphine in Supportive Oncology and Palliative Care

Opioid Naïve	• Low dose TD buprenorphine • Ideal for older adults
Low dose breakthrough	• We do not titrate below 30 mg OME • Use buprenorphine as "long-acting"
At risk of opioid use disorder	• Use buprenorphine as "long-acting" • Limit use of full agonist opioids where possible

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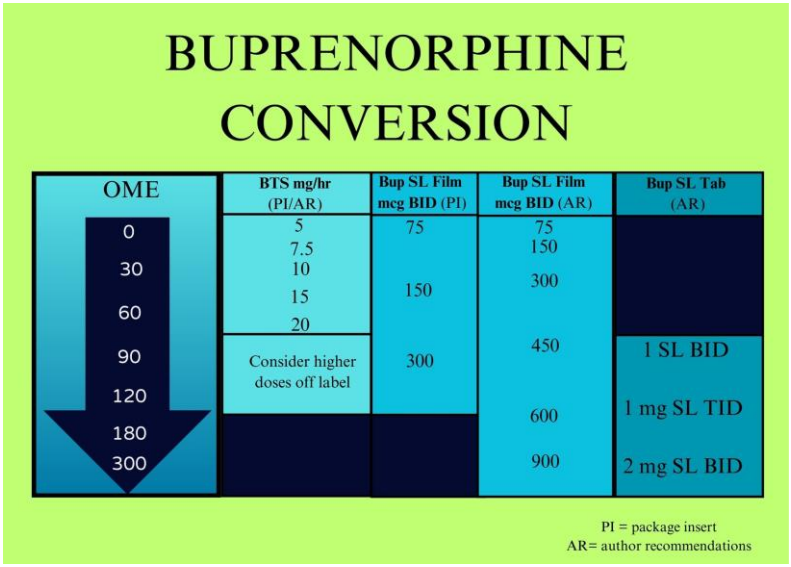
Titration and Dose Conversion



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Buprenorphine to the Rescue!

- In the setting of non-medical opioid use and cancer-related pain co-exist
- In those who are exquisitely sensitive to full agonist opioids
- In head and neck cancer for those undergoing radiation and concurrent chemo-radiation
- In those patients who “don’t like taking these sorts of meds” (particularly good for transdermal buprenorphine)

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Buprenorphine Barriers

- Concerns from patients
  - "Isn't this for addicts?"
  - "It's a blocker!"
  - "My family said I'll never get off this stuff."
- Pharmacists calling regarding an "interaction" with full agonist opioids
- Insurance companies insisting upon starting full agonist opioids first!

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Studying Buprenorphine with Full Agonist Opioids

- Background
  - Expert consensus suggest decrease of full agonist opioids to less than 30 oral morphine equivalents.
- Hypothesis
  - We hypothesized, especially in the advent of micro-dosing that using buprenorphine products with full agonist opioids would not require tapering below 30 oral morphine equivalents
- Methods
  - Recruiting 50 patients on buprenorphine and full agonist opioids at doses > 30 OME. Bi-weekly contact for 12 weeks to assess pain and withdrawal symptoms (using modified COWS score)
  - Retrospective Review of 50 patients who met the same criteria

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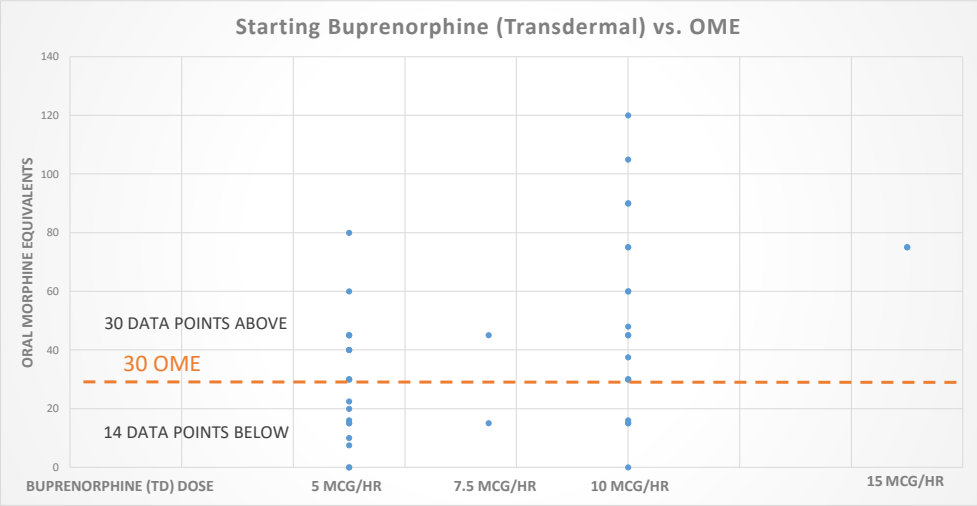
Retrospective Review



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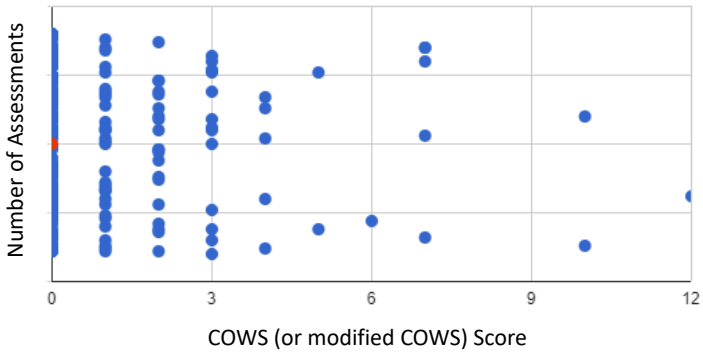
Clinical Opiate Withdrawal Score

- 33 Recruited Patients (plan for 50)
- Measuring COWS every 2 weeks while on study (84 days total)
- Overlap between cancer/treatment related symptoms and withdrawal (anxiety, sweating, diarrhea)
- Median is O (193 data points thus far)



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A couple interesting points…

While data not full analyzed (and we lack the power)—a couple things we have noticed:

- Many patients on low dose full agonist opioids, often greatly reduce or even stop the full agonist opioids.
- Hydromorphone seems to work the best (? Higher binding capacity) with buprenorphine
- Patients often have zero or limited side effects (mental "fog" or nausea)
  - Some are intolerant to buprenorphine due to headache, overwhelming, nausea, or "I just don't feel right"
- Insurance can often be convinced to start buprenorphine as a first-line.
- We have been successful in getting higher doses (up to 40 mcg/hr) approved.

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Conclusions and Future Directions

- Buprenorphine is our first line analgesic for cancer-related pain
- Preliminary results of our study of combining buprenorphine and full agonist opioids show no significant withdrawal symptoms and often show a decrease in full agonist opioid use
- As many of our patients end up on LTOT, buprenorphine is a key tool to help decrease full agonist opioids and minimize long-term risks of opioid therapy.

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References

1. Falzone L, Salomone S, Libra M. Evolution of cancer pharmacological treatments at the turn of the third millennium. *Front Pharmacol*. 2018;9:1300. doi:10.3389/fphar.2018.01300
2. From Cancer Patient to Cancer Survivor: Lost in Transition; National Academies Press: Washington, D.C., 2005. https://doi.org/10.17226/11468.
3. Wiffen, P. J.; Wee, B.; Derry, S.; Bell, R. F.; Moore, R. A. Opioids for Cancer Pain - an Overview of Cochrane Reviews. Cochrane Database Syst. Rev. 2017, 7 (7), CD012592.
4. Caraceni, A.; Hanks, G.; Kaasa, S.; Bennett, M. I.; Brunelli, C.; Cherny, N.; Dale, O.; De Conno, F.; Fallon, M.; Hanna, M.; Haugen, D. F.; Juhl, G.; King, S.; Klepstad, P.; Laugsand, E. A.; Maltoni, M.; Mercadante, S.; Nabal, M.; Pigni, A.; Radbruch, L.; Reid, C.; Sjogren, P.; Stone, P. C.; Tassinari, D.; Zeppetella, G.; European Palliative Care Research Collaborative (EPCRC); European Association for Palliative Care (EAPC). Use of Opioid Analgesics in the Treatment of Cancer Pain: Evidence-Based Recommendations from the EAPC. Lancet Oncol. 2012, 13 (2), e58-68.
5. Manhapra, A. Complex Persistent Opioid Dependence—an Opioid-Induced Chronic Pain Syndrome. Curr. Treat. Options Oncol. 2022, 23 (7), 921–935

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8. Davis MP. Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain. J Support Oncol. 2012 Nov-Dec;10(6):209-19. doi: 10.1016/j.suponc.2012.05.002. Epub 2012 Jul 17. PMID: 22809652.

21

References (continued)

9. Miller, J. C., Brooks, M. A., Wurzel, K. E., Cox, E. J., & Wurzel, J. F. (2023). A guide to expanding the use of buprenorphine beyond standard initiations for opioid use disorder. *Drugs in R&D*.

10. Pace, M. C., Passavanti, M. B., Grella, et al. (2007). Buprenorphine in long-term control of chronic pain in cancer patients. Frontiers in Bioscience, 12, 1291–1299.

11. Wolff, R. F., Aune, D., Truyers, C., et al (2012). Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. Current Medical Research and Opinion, 28(5), 833–845.

12. Corli, O., Floriani, I., Roberto, A., et al. (2016). Are strong opioids equally effective and safe in the treatment of chronic cancer pain? A multicenter randomized phase IV “real life” trial on the variability of response to opioids. Annals of Oncology, 27(6), 1107–1115.

13. Melilli G, Samolsky Dekel BG, Frenquelli C, et al. Transdermal opioids for cancer pain control in patients with renal impairment. J Opioid Manag. 2014;10(2):85-93.

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