

DOWIERCIAŁ, Kinga, WZIĘTEK, Joanna, KOWALIK, Piotr, KRZYŻANOWSKA, Daria, Fatyga, Patrycja, Fatyga, Wiktoria, PABIS, Gabriela, BĘTKOWSKA, Paula, KOZIOŁEK, Iwona and STRZELCZYK, Magdalena. Ketamine in palliative care: an updated systematic review. *Quality in Sport.* 2025;43:61429. eISSN 2450-3118.

<https://doi.org/10.12775/QS.2025.43.61429>
<https://apcz.umk.pl/QS/article/view/61429>

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024. No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2025.

This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland. Open Access: This article is distributed under the terms of the Creative Commons Attribution Noncommercial License, which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits unrestricted, non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interest regarding the publication of this paper.

Received: 25.05.2025. Revised: 05.07.2025. Accepted: 05.07.2025. Published: 08.07.2025.

Ketamine in palliative care: an updated systematic review

Kinga Dowierniał, Joanna Wziętek, Piotr Kowalik, Daria Kryżanowska, Patrycja Fatyga, Wiktoria Fatyga, Gabriela Pabis, Paula Bętkowska, Iwona Koziołek, Magdalena Strzelczyk

Authors:

Kinga Dowierniał [KD]

Independent Public Regional Specialist Hospital in Chełm, Ceramiczna 1 Street,
22-100 Chełm, Poland

kinga.dowiercial@gmail.com

<https://orcid.org/0009-0000-9132-1026>

Joanna Wziętek [JW]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street,
93-113 Łódź, Poland

wziatek.joanna1@gmail.com

<https://orcid.org/0009-0002-1656-7477>

Piotr Kowalik [PK]

Medical University of Lodz, Tadeusz Kościuszko Avenue 4,
90-419 Lodz

piotrek.kowalik14@gmail.com

<https://orcid.org/0009-0009-4813-9742>

Daria Kryżanowska [DK]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street,
93-113 Łódź, Poland

dariakrzym@wp.pl

<https://orcid.org/0009-0002-5349-5679>

Patrycja Fatyga [PF]

The Provincial Hospital, Grunwaldzka 45,
25-736 Kielce, Poland,
patrycja3.fatyga@gmail.com
<https://orcid.org/0009-0001-1277-1246>

Wiktoria Fatyga [WF]

Non-public Health Care Facility Prophylactics Wiesława Piotrowska Limited Liability Company, Jana Jeziorskiego 137,
25-432 Kielce, Poland
wiktoria.fatyga34@gmail.com
<https://orcid.org/0009-0000-5931-925X>

Gabriela Pabis [GP]

The Provincial Hospital, Grunwaldzka 45,
25-736 Kielce, Poland
gabriela.pabis98@gmail.com
<https://orcid.org/0009-0002-3208-5160>

Paula Bętkowska [PB]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street,
93-113 Łódź, Poland
paula.betkowska0306@gmail.com
<https://orcid.org/0009-0002-7050-4039>

Iwona Koziolek [IK]

The Provincial Hospital, Grunwaldzka 45,
25-736 Kielce, Poland,
bajor-iwona@wp.pl
<https://orcid.org/0009-0002-1077-3640>

Magdalena Strzelczyk [MS]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street,
93-113 Łódź, Poland
strzelczykmagdamed@gmail.com
<https://orcid.org/0009-0005-6312-3002>

ABSTRACT

Introduction

Ketamine is a well-known anesthetic and analgesic agent which primarily works through N-methyl-D-aspartate (NMDA) receptor antagonism, offering powerful analgesic effects that is particularly useful in opioid-refractory pain. Beyond pain control, it garnered significant attention in depression and anxiety research, which are some of the most frequent and serious symptoms experienced by patients in need of palliative care. This article provides an overview of Ketamine therapeutic applications in treatment of depression, anxiety, physical pain, opioid tolerance and opioid-induced hyperalgesia (OIH), drawing on research from PubMed published between 2020 and 2025.

Aim of study

This review aims to present the current state of knowledge regarding Ketamine, focusing on its pharmacological properties, clinical applications, and potential role in palliative care.

Material and methods

The review was based on research of articles published from 2020 to 2025 on the PubMed database. Keywords used in research were among others: Ketamine, palliative care, pain, neuropathic pain, depression.

Current state of knowledge

Ketamine plays important role in anesthesiology and it shows a lot of potential in psychiatry. Multifactorial effects result from complex mechanism of action. Evidence suggests Ketamine can be effective in managing refractory pain (enabling lower doses of opioids even in severe pain), depression and anxiety disorders, opioid tolerance and OIH, positioning ketamine as a promising agent for palliative care.

Summary (conclusions)

Ketamine's advantages such as its rapid onset, wide range applications, favorable safety profile at subanesthetic doses and many routes of administration make it a valuable tool in the end-of-life care. However long term studies are crucial for identifying both benefits and possible risks.

Keywords: Ketamine, pain, palliative care, depression, anxiety, OIH, opioid tolerance

INTRODUCTION

Palliative care, according to the WHO definition, is a form of care for people living with serious illnesses, regardless of diagnosis or prognosis, which focuses on relieving symptoms and reducing suffering caused by the illness. The goal of palliative care is to improve the quality of life of patients and their loved ones, so they can live as fully as possible despite the limitations imposed by the disease. Effective treatment of ailment allows meeting patient's higher needs- psychosocial, spiritual, existential.

Ketamine is a derivative of phencyclidine (PCP) that acts primarily as a non-competitive NMDA (N-methyl-D-aspartate) receptor antagonist, a subtype of glutamate receptor in the central nervous system. First synthesized in 1962 and approved for clinical use in 1970, ketamine was initially used exclusively as a dissociative anesthetic, valued for its unique properties: the ability to induce anesthesia, amnesia, and sedation while preserving airway protective reflexes and maintaining hemodynamic stability due to its sympathomimetic effects. [1] This drug is also distinguished by its analgesic properties (as the only currently used intravenous anesthetic with this feature), enabling its use in monoanesthesia and low-opioid anesthesia. These characteristics have made it a valuable agent across various medical fields, including emergency medicine, anesthesia induction, and pediatric procedures. [2]

In recent years, Ketamine has regained interest in neuropsychiatry due to its rapid-acting antidepressant effects, particularly in patients with treatment-resistant depression (TRD) and acute suicidal ideation. This rapid therapeutic response is likely mediated through glutamatergic neurotransmission modulation, enhanced synaptic plasticity, and effects on neurotrophic signaling pathways such as BDNF (brain-derived neurotrophic factor) and the mTOR (mammalian target of rapamycin) pathway. [3]

Despite its clinical potential, psychotomimetic effects, addiction risk, and adverse effects necessitate careful evaluation of Ketamine's long-term safety profile and may limit its use in palliative care. Ongoing research aims to elucidate its precise mechanisms of action, optimize dosing regimens, and develop analogues or related compounds, and hopefully will enable broader therapeutic applications. [4]

The review aims to highlight innovative, multidirectional applications of Ketamine in palliative care and to show present barriers and need for further research in this area.

The review is based on the latest articles from the PubMed database in the years 2020-2025.

Keywords like Ketamine, pain, palliative care, depression, anxiety, OIH, opioid tolerance were used in the search.

ADVANTAGES AND DISADVANTAGES OF KETAMINE [2,4]

Advantages	Disadvantages
<ul style="list-style-type: none">• Flexible administration (IV, subcutaneous, oral, or intranasal routes available).• Rapid and versatile relief• Cardiovascular stability• reduction of airway resistance and relaxation of airway smooth muscle• Minimal respiratory depression (safer than opioids in some cases).• May improve mood and quality of life.• Anti-Inflammatory properties	<ul style="list-style-type: none">• Psychotomimetic effects (hallucinations, dissociation) may require dose adjustments.• Limited long-term safety data in palliative populations.• Requires careful patient selection and monitoring.• Elevates intracranial pressure, risk of increased cerebral blood flow (this effect have not been confirmed in more recent studies).• Risk of abuse

CLINICAL USE

Physical pain

Pain treatment represents one of the most critical area in palliative medicine. Among oncology patients, pain is highly prevalent, occurring in up to 50.7% of cases across all cancer stages. [5] Within this population, conventional pharmacological management fails to provide adequate pain control in 20-40% of patients. [6] Ketamine is a unique anesthetic agent that has gained prominence primarily due to its analgesic properties, specifically in treating both acute and chronic pain, including cases resistant to standard therapies. [7] Moreover, use of additional drugs with Ketamine, such as magnesium infusion may significantly improving analgesia. [4] Originally developed in the 1960s, its analgesic effect comes from stimulating μ -opioid and κ -opioid receptors. Unique mechanism of action and multi-target effects on pain pathways make it important drug in managing complex pain syndromes, primarily as a co-analgesic. [8] Ketamine has proven to be an effective analgesic for nociceptive (tissue-related), neuropathic (nerve-related) and inflammatory pain.[9] In palliative care an important issue is refractory cancer pain. The medical literature defines refractory cancer pain as pain related to malignant disease or its treatment persistent for at least three months, resistant to appropriate analgesic therapy including opioids, adjuvant analgesics, non-pharmacological interventions. Ketamine benefits oncology patients with treatment-resistant pain, proving particularly significant for opioid-refractory cases, particularly in uncontrolled neuropathic pain. [6] However, divergence of opinion regarding the usefulness of subanesthetic Ketamine for managing opioid refractory cancer pain were noted and investigators acknowledged the lack of high-quality trials. [10,11] Anti-inflammatory properties enhance its efficacy in chronic pain through inhibition of pro-inflammatory cytokines, reduction of glial cell activation, attenuation of oxidative stress. [10] As an opioid adjunct Ketamine enables opioid dose reduction and improves overall pain control. [12] Its particularly effective for managing

neuropathic cancer pain that can be caused by tumor growth, nerve compression, tissue infiltration and chemotherapy/radiotherapy side effects. [13]

Opioid tolerance and Opioid-induced hyperalgesia (OIH)

Opioid-induced hyperalgesia (OIH) is a state of heightened pain sensitivity caused by opioid use. Unlike tolerance (reduced opioid effect), OIH leads to a paradoxical increase in pain perception, where patients on opioids may experience enhanced sensitivity to painful stimuli or new or worsening pain, different from the original condition.[14] Currently, there are limited reports on the occurrence of opioid-induced hyperalgesia (OIH) among cancer patients, but it is believed that this phenomenon may be underdiagnosed and underreported in this population.[15] Key mechanisms involve neuroplastic changes in the central nervous system, particularly NMDA receptor activation and central sensitization.[16] Opioids remain the cornerstone of analgesic therapy for patients receiving palliative care. However, chronic opioid use can lead to reduced analgesic efficacy (tolerance) and paradoxical pain hypersensitivity (opioid-induced hyperalgesia, OIH). Ketamine's mechanisms of action in treating OIH and opioid tolerance are: enhancing opioid receptor signaling, reducing opioid-induced desensitization, blocking NMDA receptors involved in central sensitization – a key mechanism underlying opioid tolerance and OIH. Ketamine therapy presents a potentially safer alternative to conventional strategies for managing opioid tolerance, which include dose escalation, opioid rotation, adjuvant analgesics. Increasing opioid doses is particularly risky due to the intensification of side effects, risk of overdose, and addiction. [14,16]. Preclinical Evidence shows that multiday intravenous ketamine infusions have demonstrated the ability to "reset" μ -opioid receptors (MORs), restoring sensitivity for several weeks, enable opioid dose reduction while maintaining effective analgesia.[15,17] Important consideration is that according to some studies, Ketamine's efficacy may vary depending on the specific opioid medication used in therapy. [16,18]

Depression

Major depressive disorder (MDD) is a significant problem in patients with advanced cancer, receiving palliative care, with an estimated prevalence of 10–15%. [19] It has been proven that MDD is an independent risk factor for poor prognosis, associated with reduced survival in patients with cancer. Depressive symptoms often coexist with existential distress and death anxiety, and may negatively impact pain severity in patients with advanced cancer. [20] Early and effective treatment of depression is crucial to reducing end-of-life suffering and improving the quality of life of patients. Glutamatergic agents, particularly ketamine, represent a new class of antidepressant medications. The growing popularity of glutamatergic drugs in the treatment of depression stems from their significantly faster onset of action, higher efficacy in patients resistant to conventional treatments, and a unique mechanism of action involving modulation of the glutamatergic system. [21,22] Additionally, ketamine exhibits a rapid effect on suicidal thoughts. [23] It appears to be particularly effective when used alongside psychotherapy, with a reduced risk of psychomimetic side effects.[24] Intranasal Esketamine has been approved for the treatment of depression by the U.S. Food and Drug Administration (FDA) and other regulatory agencies. [22] Ketamine currently remains an off-label treatment for treatment-resistant depression (TRD). [25] The response rate to treatment is 65–70%, which is higher than that of classical antidepressants.[23] The onset of action is rapid- effects

may appear within less than one hour after subcutaneous administration, with maximum antidepressant effects observed approximately 24 hours post-dose and lasting up to 7 days. [26] In the case of oral administration, the onset of action is delayed.[27] Possible side effects such as dissociation, hallucinations, and dysphoria require careful dose selection and may sometimes necessitate the use of adjunctive medications (e.g., benzodiazepines, Clonidine or Haloperidol). [21]

Anxiety

Life-threatening terminal illnesses affect physical, emotional, social, and spiritual well-being. Psychiatric disorders are prevalent, with anxiety disorders estimated to occur in approximately 10% of cancer patients receiving palliative care. Research demonstrates that the dissociative anesthetic ketamine - even in single doses - exhibits rapid anxiolytic and mood-enhancing effects.[28] Unlike conventional antidepressants and anxiolytics which require weeks to take effect, Ketamine produces clinically significant improvement within hours, with effects lasting for days or weeks which makes them a potential alternative to benzodiazepines. [29] In contrast to benzodiazepines Ketamine does not result in physical dependence as its discontinuation does not produce withdrawal symptoms (although there is still a low risk of psychological dependence) [4]. Therefore, Ketamine may provide therapeutic benefits for patients with treatment-resistant anxiety disorders where other conventional anxiolytics have proven ineffective. [30,31] However, the role of NMDA receptors in anxiety reduction remains relatively poorly understood.

CONCLUSIONS

Ketamine offers rapid and effective treatment for depression, particularly in patients who have not responded to first- line medications, and shows promise in managing anxiety disorders. It serves as a crucial intervention in severe cases, especially when suicidal thoughts are present, where the speed of therapeutic effect is particularly important. Ongoing research aims to determine the optimal dosing, strategies for maintaining treatment effects, and the long-term safety of its use.

Ketamine may also serve as an adjunctive therapy in reducing opioid tolerance and alleviating hyperalgesia. A key benefit is that patients continue to receive adequate analgesia during treatment. However, its use should be guided by clinical evidence and individual patient assessment. Further research is needed to refine dosing protocols and confirm the safety of long-term use.

The main issue is that the reported effects of ketamine in the treatment of the aforementioned conditions are still based, at least in part, on a small number of studies and participants. There is a lack of larger, more rigorous trials to confirm these findings. Some studies involve small patient groups, which further emphasizes the need for replication. In addition, variability in the doses used, frequency of administration, and duration of treatment can influence outcomes and should be carefully considered when designing studies and interpreting their results.

In summary, the multifaceted action of Ketamine makes it a valuable adjunct in palliative care. Research particularly highlights its rapid onset of action and effectiveness in cases where standard treatments fail to yield

satisfactory results. Its ability to alleviate both physical and psychological suffering makes it a unique option for improving quality of life at the end of life. It appears, that with the careful assessment, monitoring, and a personalized approach Ketamine may be safely and effectively integrated into palliative care to enhance outcomes and with reducing potential risks While not a first-line treatment, ketamine should be considered more frequently as an option in palliative care.

Disclosures

Patient consent: Not applicable.

Data were obtained from: PubMed

Author's contribution: Conceptualization: KD, MS, GP; Methodology: IK, PF, JW; Software: WF, PF, PB; Check: KD, JW, DK; Formal analysis: GP, IK, PB; Investigation: PK, WF, MS; Resources: IK, PK, JW; Data curation: MS, WF, PB; Writing-rough preparation: IK, GP, JW; Writing-review and editing: KD, DK, PK; Visualization: PF, WF, GP ; Supervision: PB, MS, DK; Project administration: PF, DK, KD

All authors have read and agreed with the published version of the manuscript.

Funding statement: The study has not received any external funding.

Ethical approval: Not applicable.

Statement of institutional review board: Not applicable.

Statement of informant consent: Not applicable.

Statement of data availability: Not applicable.

Conflict of interest statement: The authors declare no conflict of interest.

REFERENCES

1. Reed JR, Parks SK, Kaniaru A, Hefley J, Yauger Y, Edwards JV, Glymph DC. Ketamine Use for Palliative Care in the Austere Environment: Is Ketamine the Path Forward for Palliative Care. *Am J Hosp Palliat Care.* 2025 Mar;42(3):225-229. Epub 2024 Apr 17. PMID: 38631682 <https://doi.org/10.1177/10499091241246520>

2. Midega TD, Chaves RCF, Ashihara C, Alencar RM, Queiroz VNF, Zelezoglo GR, Vilanova LCDS, Olivato GB, Cordioli RL, Bravim BA, Corrêa TD. Ketamine use in critically ill patients: a narrative review. *Rev Bras Ter Intensiva.* 2022 Apr-Jun;34(2):287-294. PMID: 35946660 <https://doi.org/10.5935/0103-507x.20220027-pt>
3. Johnston JN, Kadriu B, Kraus C, Henter ID, Zarate CA Jr. Ketamine in neuropsychiatric disorders: an update. *Neuropsychopharmacology.* 2024 Jan;49(1):23-40. Epub 2023 Jun 20. PMID: 37340091 <https://doi.org/10.1038/s41386-023-01632-1>
4. Riccardi A, Guarino M, Serra S, Spampinato MD, Vanni S, Shiffer D, Voza A, Fabbri A, De Iaco F; Study and Research Center of the Italian Society of Emergency Medicine. Narrative Review: Low-Dose Ketamine for Pain Management. *J Clin Med.* 2023 May 2;12(9):3256. PMID: 37176696 <https://doi.org/10.3390/jcm12093256>
5. Patel S, Tatachar V, Singh AB, Galea J, Fattakhov E, Kaur G. Low-dose ketamine as an adjuvant for pain control in a cancer patient: a case report. *Ann Palliat Med.* 2021 Jul;10(7):8328-8333. Epub 2021 Feb 8. PMID: 3361580 <https://doi.org/10.21037/apm-20-1685>
6. Cheung KWA, Chan PC, Lo SH. The use of ketamine in the management of refractory cancer pain in a palliative care unit. *Ann Palliat Med.* 2020 Nov;9(6):4478-4489. Epub 2019 Oct 9. PMID: 31594372 <https://doi.org/10.21037/apm.2019.09.09>
7. Tagami K, Matsuoka H, Ariyoshi K, Oyamada S, Hiratsuka Y, Kizawa Y, Koyama A, Inoue A. The current clinical use of adjuvant analgesics for refractory cancer pain in Japan: a nationwide cross-sectional survey. *Jpn J Clin Oncol.* 2020 Dec 16;50(12):1434-1441. PMID: 32869060 <https://doi.org/10.1093/jco/hyaa147>
8. Schauer SG, Naylor JF, Davis WT, Borgman MA, April MD. An Analysis of Prolonged, Continuous Ketamine Infusions. *Mil Med.* 2022 May 3;187(5-6): e547-e553. PMID: 33492388 <https://doi.org/10.1093/milmed/usaa481>
9. Winegarden JA, Carr DB, Bradshaw YS. Topical Ketamine with Other Adjuvants: Underutilized for Refractory Cancer Pain? A Case Series and Suggested Revision of the World Health Organization Stepladder for Cancer Pain. *J Palliat Med.* 2020 Sep;23(9):1167-1171. Epub 2020 Mar 11. PMID: 32167846 <https://doi.org/10.1089/jpm.2019.0618>

10. Poon P, Bell RF, Good P. Should Subanesthetic Ketamine be Considered When Managing Opioid Refractory Cancer Pain? *J Pain Symptom Manage.* 2024 Aug;68(2): e146-e151. Epub 2024 May 8. PMID: 38729533 <https://doi.org/10.1016/j.jpainsympman.2024.04.026>
11. Chang J, Edmonds KP, Atayee RS. A National Survey of Institutional Guidelines for the Use of Ketamine, Lidocaine, and Dexmedetomidine for Refractory Pain. *J Palliat Med.* 2023 Jul;26(7):986-991. Epub 2023 Apr 19. PMID: 37074348 <https://doi.org/10.1089/jpm.2023.0022>
12. Nath TS. Effectiveness of Low-Dose Ketamine Infusion in Opioid Refractory Cancer Pain: A Case Report. *Cureus.* 2022 Nov 18;14(11):e31662 .eCollection 2022 Nov. PMID: 36545179 <https://doi.org/10.7759/cureus.31662>
13. Kouri M, Rekatsina M, Vadalouca A, Siafaka I, Vardas E, Papadopoulou E, Paladini A, Varrassi G. Pharmacological Management of Neuropathic Pain after Radiotherapy in Head and Neck Cancer Patients: A Systematic Review. *J Clin Med.* 2022 Aug 19;11(16):4877. PMID: 36013118 <https://doi.org/10.3390/jcm11164877>
14. Xie WJ, Hong JS, Feng CF, Chen HF, Li W, Li YC. Pharmacological interventions for preventing opioid-induced hyperalgesia in adults after opioid-based anesthesia: a systematic review and network meta-analysis. *Front Pharmacol.* 2023 Jun 22;14:1199794. eCollection 2023. PMID: 37426819 <https://doi.org/10.3389/fphar.2023.1199794>
15. Hino C, Ran-Castillo D, Akhtari M, Cao H, Silvestre J. Role of Ketamine and Opioid Rotation in the Management of Opioid Induced Hyperalgesia in a Patient with Acute Promyelocytic Leukemia. *J Oncol Pharm Pract.* 2022 Jul;28(5):1254-1258. Epub 2022 Jan 24. PMID: 35068247 <https://doi.org/10.1177/1078155221074285>
16. Viisanen H, Lilius TO, Sagalajev B, Rauhala P, Kalso E, Pertovaara A. Neurophysiological response properties of medullary pain-control neurons following chronic treatment with morphine or oxycodone: modulation by acute ketamine. *J Neurophysiol.* 2020 Sep 1;124(3):790-801. Epub 2020 Aug 5. PMID: 32755331 <https://doi.org/10.1152/jn.00343.2020>
17. Cairns J, Feng TL, Ong MC. Continuous ketamine infusion for the management of opioid-induced hyperalgesia following amputation. *BMJ Case Rep.* 2024 Jan 4;17(1): e255333. PMID: 38176753 <https://doi.org/10.1136/bcr-2023-255333>
18. Mizobuchi Y, Miyano K, Manabe S, Uezono E, Komatsu A, Kuroda Y, Nonaka M, Matsuoka Y, Sato T, Uezono Y, Morimatsu H. Ketamine Improves Desensitization of -Opioid Receptors Induced by Repeated

Treatment with Fentanyl but Not with Morphine. *Biomolecules*. 2022 Mar 10;12(3):426. PMID: 35327617 <https://doi.org/10.3390/biom12030426>

19. Lee W, Sheehan C, Chye R, Chang S, Loo C, Draper B, Agar M, Currow DC. Study protocol for SKIPMDD: subcutaneous ketamine infusion in palliative care patients with advanced life limiting illnesses for major depressive disorder (phase II pilot feasibility study). *BMJ Open*. 2021 Jun 28;11(6):052312. PMID: 34183351 <https://doi.org/10.1136/bmjopen-2021-052312>
20. Oyetunji A, Huelga C, Bunte K, Tao R, Bellman V. Use of ketamine for depression and suicidality in cancer and terminal patients: Review of current data. *AIMS Public Health*. 2023 Jul 21;10(3):610-626. eCollection 2023. PMID: 37842268 <https://doi.org/10.3934/publichealth.2023043>
21. Simões C, Julião M, Calaveiras P, Câmara P, Santos T. Ketamine subcutaneous continuous infusion for depressive symptoms at home: A case report beyond pain use. *Palliat Support Care*. 2024 Oct;22(5):1516-1520. PMID: 38706299 <https://doi.org/10.1017/s1478951524000798>
22. Rosenblat JD, DeVries FE, Doyle Z, McIntyre RS, Rodin G, Zimmermann C, Mak E, Hannon B, Schulz-Quach C, Kindy AA, Patel Z, Li M. A Phase II, Open-Label Clinical Trial of Intranasal Ketamine for Depression in Patients with Cancer Receiving Palliative Care (INKeD-PC Study). *Cancers (Basel)*. 2023 Jan 7;15(2):400. PMID: 36672348 <https://doi.org/10.3390/cancers15020400>
23. Barbosa MG, Garcia GT, Sarin LM, Jackowski AP. Efficacy and safety of ketamine for the treatment of depressive symptoms in palliative care: A systematic review. *Braz J Psychiatry*. 2023 May 11;45(2):182-195. PMID: 36574497 <https://doi.org/10.47626/1516-4446-2022-2876>
24. Forcén FE, Marengo L, Behn M. Ketamine-assisted meaning-centered psychotherapy for a patient with severe suicidal behavior. *Palliat Support Care*. 2023 Apr;21(2):362-364. PMID: 36193694 <https://doi.org/10.1017/s1478951522001304>
25. Jelen LA, Stone JM. Ketamine for depression. *Int Rev Psychiatry*. 2021 May;33(3):207-228. Epub 2021 Feb 11. PMID: 33569971 <https://doi.org/10.1080/09540261.2020.1854194>
26. Barbosa MG, Delfino RS, Sarin LM, Jackowski AP. Repeated subcutaneous esketamine administration for depressive symptoms and pain relief in a terminally ill cancer patient: A case report. *Palliat Med*. 2020 Jun;34(6):822-825. Epub 2020 Mar 18. PMID: 32186250 <https://doi.org/10.1177/0269216320910351>
27. Latuga NM, Luczkiewicz DL, Grant PC, Levy K, Hansen E, Kerr CW. Single Subcutaneous Ketamine Dose Followed by Oral Ketamine for Depression Symptoms in Hospice Patients: A Case Series. *J Pain Palliat Care Pharmacother*. 2021 Jun;35(2):106-112. Epub 2021 Apr 13. PMID: 33847212 <https://doi.org/10.1080/15360288.2021.1883182>

28. Sholevar R, Kromka W, Beaussant Y. Ketamine and Ketamine-Assisted Psychotherapy for Psychiatric and Existential Distress in Patients with Serious Medical Illness: A Narrative Review. *J Palliat Med.* 2025 Jan 22. PMID: 39841075 <https://doi.org/10.1089/jpm.2024.0346>
29. Tully JL, Dahlén AD, Haggarty CJ, Schiöth HB, Brooks S. Ketamine treatment for refractory anxiety: A systematic review. *Br J Clin Pharmacol.* 2022 Oct;88(10):4412-4426. Epub 2022 May 20. PMID: 35510346 <https://doi.org/10.1111/bcp.15374>
30. Banov MD, Young JR, Dunn T, Szabo ST. Efficacy and safety of ketamine in the management of anxiety and anxiety spectrum disorders: a review of the literature. *CNS Spectr.* 2020 Jun;25(3):331-342. Epub 2019 Jul 24. PMID: 31339086 <https://doi.org/10.1017/s1092852919001238>
31. Glue P, Neehoff S, Beaglehole B, Shadli S, McNaughton N, Hughes-Medlicott NJ. Ketamine for treatment-resistant major depressive disorder: Double-blind active-controlled crossover study. *J Psychopharmacol.* 2024 Feb;38(2):162-167. Epub 2024 Jan 31. PMID: 38293803 <https://doi.org/10.1177/02698811241227026>