Updating Extemporaneous Chemotherapy Compounding Guidelines and Assessing Alternative Routes of Administration of Oral Oncology Drugs

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Introduction

- Oral chemotherapy has become increasingly integrated into oncology practice and continues to be an attractive treatment modality due to improved outcomes in some cancers and convenient oral administration[1]

With many oral oncology drugs (OODs) approved and many more in development, these small-molecule inhibitors hold a valuable place as targeted anti-cancer therapy in multiple diseases.

Dysphagia in Cancer Patients and Enteral Drug Administration

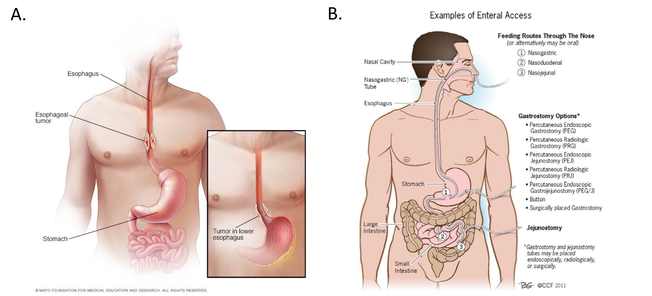

Figure 1.
(A) Oropharyngeal dysphagia in esophageal cancer; (B) Enteral tube feeding access options

Despite the marked growth in OOD development, there remains a significant gap in knowledge of administering these agents for patients unable to tolerate solid oral formulations.

- May be due to swallowing challenges, anatomical changes secondary to the cancer, or nutritionally-related support needs
- Multifactorial etiology in patients with head and neck cancer[2]
- Swallowing deficits also present for patients requiring enteral nutrition (nasoenteric or enterostomy feeding) and many OODs not approved for administration via feeding tube

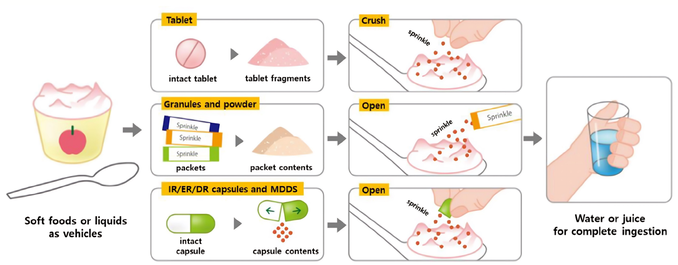

Figure 2.
Main drug preparations/reformulations to facilitate administration in dysphagic patients

Research Objective

This study assesses the current literature, drug information resources, and manufacturer-supplied medical information to evaluate currently and newly approved OODs for their potential to be safely reformulated for administration to patients unable to swallow solid dosage forms.

Methods

1. Preliminary search to assess OOD availability conducted on FDA's "*Novel Drug Approvals*" website starting from January 2015 through December 2022. Results consolidated with previous review conducted in 2022.[3]
2. Tertiary resources, including Lexicomp, Micromedex, DailyMed, and OHSU's institutional Drug Information/Healthcare Policy databases searched to locate additional information on evaluating OOD excipients that could prevent effective enteral administration.
3. Primary literature search conducted through PubMed and Ovid MEDLINE databases to search for additional information on extemporaneous preparations of OODs and stability data on reformulations.
4. Similar inquiry completed using digital copies of *ASPEN's Guidebook on Enteral Medication Administration* and the *Handbook of Drug Administration via Enteral Feeding Tubes*.
5. Individual OOD manufacturers were contacted via phone, email, or using online inquiry forms submitted through manufacturers' respective medical information websites. Any follow-up completed on an as-needed basis.

Discussion

- Presence of OOD excipients (e.g., hypromellose) hinder effective extemporaneous compounding and complicate enteral administration by clogging feeding tubes
  - Potential solutions to prevent thickening: regular flushing and ensuring compounded formulation has appropriate BUD[4]
- Research served to provide annual update to institutional extemporaneous compounding guidelines for OODs
  - In practice, an algorithm, as represented in *Figure 3*, paired with such guidelines can help further optimize clinical workflows

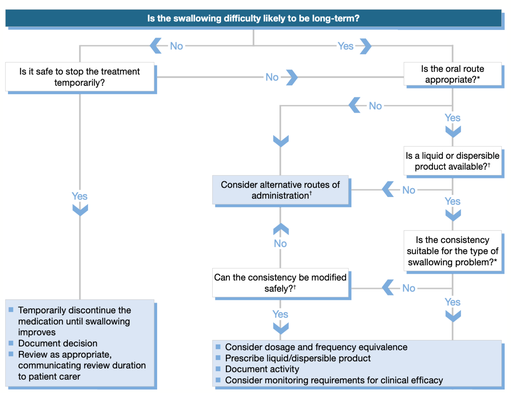

Figure 3.
General clinical algorithm for medication management of adult patients with dysphagia
Seek advice from multidisciplinary care team including referral to ENT Service:
** Speech-language pathologist +/- occupational therapist, physical therapist, or dietitian if included in dysphagia management*
† Clinical pharmacist; assesses need for drug reformulation/extemporaneous compounding on a patient-specific basis

Results

- A total of 128 OODs were reviewed to assess their potential to be safely reformulated without compromising therapeutic efficacy for administration to dysphagic patients
- Majority of OODs had information describing extemporaneous compounding or alternative routes of administration (30% with commercial liquid formulations available or information in tertiary resources; 33% with off-label manufacturer-supplied medical information or case reports) while 37% had no data

A.

abemaciclib	dacomitinib	lenvatinib	relugolix
abiraterone	darolutamide	letrozole	ribociclib
acalabrutinib	dasatinib	leucovorin	ripretinib
adagrasib	decitabine/cedazuridine	lomustine	rucaparib
afatinib	duvelisib	lorlatinib	ruxolitinib
alectinib	eltrombopag	lusutrombopag	selinexor
alpelisib	enasidenib	megestrol acetate	selpercatinib
altretamine	encorafenib	melphalan	selumetinib
anastrozole	entrectinib	mercaptopurine	sonidegib
apalutamide	enzalutamide	mesna	sorafenib
asciminib	erdafitinib	methotrexate	sotorasib
avapritinib	erlotinib	midostaurin	sunitinib
avatrombopag	estramustine	mitotane	talazoparib
axitinib	etoposide	mobocertinib	tamoxifen
azacytidine	everolimus	neratinib	tazemetostat
belumosudil	exemestane	nilotinib	temozolomide
beltuxifan	fedratinib	nilutamide	tepotinib
bexarotene	flutamide	niraparib	thalidomide
bicalutamide	fostamatinib	olaparib	thioguanine
binimetinib	futibatinib	olutasidenib	tivozanib
bosutinib	gefitinib	osimertinib	topotecan
brigatinib	gilteritinib	pacritinib	toremifene citrate
busulfan	glasdegib	palbociclib	trametinib
cabozantinib	hydroxyurea	panobinostat	tretinoin
capecitabine	ibrutinib	pazopanib	trifluridine/tipiracil
capmatinib	idelalisib	pemigatinib	tucatinib
ceritinib	imatinib	pexidartinib	vandetanib
chlorambucil	ivosidenib	pomalidomide	vemurafenib
cobimetinib	ixazomib	ponatinib	venetoclax
crizotinib	lapatinib	pralsetinib	vismodegib
cyclophosphamide	larotrectinib	procarbazine	vorinostat
dabrafenib	lenalidomide	regorafenib	zanubrutinib

B.

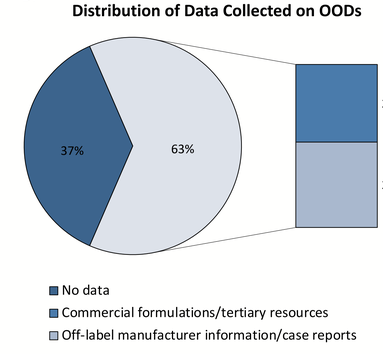

Figure 4.
(A) List of OODs reviewed; (B) Percentage distribution of current available data for OODs

Conclusions & Future Directions

- Research informs current institutional practices by updating the OHSU compounding protocol for inpatient use of extemporaneous oral liquid preparations of OODs
- Guideline provides comprehensive review of OOD stability data and relevant properties
  - Expedites patient care by reducing time and resources spent to evaluate new requests on an agent-specific basis
  - Optimizes current and future state compounding workflows for patients unable to tolerate solid oral formulations
- More data needed regarding physicochemical properties of different excipients, such as hypromellose and derivatives
  - Develop strategies to prevent physical instability during resuspension and optimizing physical and chemical stability for convenient length of time

References & Acknowledgments

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Images (cited in order, from left to right):
- *Figure 1a*: Esophageal cancer. Mayo Clinic. April 19, 2022. Accessed October 18, 2023. https://www.mayoclinic.org/diseases-conditions/esophageal-cancer/symptoms-causes/syc-20356084.
- *Figure 1b*: Kirby DF, Parisian K. Enteral and parenteral nutrition. September 2011. Accessed October 18, 2023. https://gi.org/topics/enteral-and-parenteral-nutrition/.
- *Figure 2*: Lee HS, Lee JJ, Kim MG, et al. Sprinkle formulations-A review of commercially available products. *Asian J Pharm Sci*. 2020;15(3):292-310. doi:10.1016/j.ajps.2019.05.003. Open access (CC BY-NC-ND).
- *Figure 3*: Wright D, Chapman N, Foundling-Miah M, et al. *Algorithm for the Medication Management of Adults with Swallowing Difficulties*. Image used with permission from Medscape UK; 2015. Accessed October 18, 2023. Available at: https://www.rosemontpharma.com/sites/default/files/20150911_adult_dysphagia_full_guideline_clean_approved_sept_15.pdf.
- Logos included in "*Methods*" section retrieved from websites of respective online drug information resources

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