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ADHERENCE IS A COMPLEX BEHAVIOR

The paradox of non-adherence to treatment in oncology

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Financial disclosure

Prof. Enrique de Madaria reports receiving consulting fees from Takeda Pharmaceutical Company Limited, fees for serving on a data and safety monitoring board from Kowa Research Institute, and travel support and lecture fees from Abbott, Janssen and Viatris.

Medical treatments in oncology

IN THE PAST	CURRENTLY
Based on IV chemotherapy	Frequent use of oral/subcutaneous drugs
Drug provided by health care facilities	Drug acquisition by the patient
Administered in health care facilities	Administered by the patient
Frequent and intense adverse events	Some drugs with few adverse events
Low efficacy, progressive disease symptoms	High efficacy, cancer as a chronic disease

Adherence in oral oncological treatments

HETEROGENEITY OF STUDIES

- Different samples (type, size)
- Different assessment methods for adherence (some of them linked to biases)
- Different definitions for adherence
- Different types of drugs: hormonal therapy, chemotherapy, immunotherapy…
- Different health care systems

1/3 studies with high risk of bias

Greer Joseph, Amoyal Nicole, *et al*. A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Adherence in oral oncological treatments

ORAL ONCOLOGICAL TREATMENT	POOR ADHERENCE
Endocrine treatment (breast, prostate)	1 week: 12%
	6 months: 15%
	1 year: 23-40%
	5 years: Up to 50%
Nonendocrine antineoplastic drugs	Baseline: Up to 36%
	1 year: 27 to 41%

Greer Joseph, Amoyal Nicole, *et al.* A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (1/7)

DEMOGRAPHIC FACTORS

Age (younger, older)

Sex (male, female)

Race (black, white)

Not married/no partner/living alone

Less education

Employment status

Lower annual income or financial status

PATIENT FACTORS

Greer Joseph, Amoyal Nicole, *et al*. A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (2/7)

PSYCHOSOCIAL AND COGNITIVE FACTORS

Lower social support

Higher depression or antidepressant use

Higher anxiety

Higher quality of life

Forgetting to take dose

Worse verbal memory

PATIENT FACTORS

Greer Joseph, Amoyal Nicole, *et al.* A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (3/7)

HEALTH RISKS AND PERCEPTIONS FACTORS

No family history of cancer

Use of alcohol and cigarettes

Greater concerns or negative emotions related to medication

Lower perceived necessity of medication

Less satisfaction with information received

Less self-efficacy in long-term medication behavior

Less knowledge of disease and treatment

PATIENT FACTORS

Greer Joseph, Amoyal Nicole, *et al.* A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (4/7)

DISEASE FACTORS

Comorbidities (more or few)	Higher cancer complexity	Suboptimal treatment/ cytogenic response or less hormone suppression
Longer duration of time since diagnosis	Worse disease severity marker	Cancer recurrence
Lower disease risk class at diagnosis	Tumor size (larger ductal cancers, smaller, unknown)	Worse survival/higher all-cause mortality
Lower tumor stage	Node-negative breast cancer	
Diagnosis of incurable cancer	Lymph node involvement	

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Risk factors for non-adherence to oral antineoplastic therapies (5/7)

TREATMENT FACTORS – MEDICATION

Higher dose	Duration of treatment (shorter or longer)
Greater toxicity/side effects/symptoms/adverse events	Adjuvant chemotherapy (presence/absence)
Medications/concomitant prescriptions (more/fewer) disease risk class at diagnosis	Combination of hormone therapy and/or radiation and/or chemotherapy
Delay of hormone treatment	Hormone replacement therapy

Greer Joseph, Amoyal Nicole, *et al.* A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (6/7)

TREATMENT FACTORS – UTILIZATION FACTORS

More long-term care received

More outpatient visits, ED visits, urgent care, hospitalizations

More tests and procedures

No attendance at regular follow-up appointments or rehabilitation program

Greer Joseph, Amoyal Nicole, *et al.* A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist* 2016;21:354-376

Risk factors for non-adherence to oral antineoplastic therapies (7/7)

TREATMENT FACTORS – UTILIZATION FACTORS

- Not seeing/less frequent/poor communication with oncologist
- More consultations/visits with oncologist
- Shorter duration of visits (initial and follow-up) with doctor
- Having a doctor with more years of professional experience
- Having a doctor not practicing in a university or teaching hospital
- Greater prescription, medical, health care, and out-of-pocket costs
- Not receiving low-income subsidy
- No use of mail-order pharmacy
- Shorter duration between prescription refills
- Non-oncologist writing prescription

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Gastrointestinal oncology and adherence

Toxicity and adherence

EXAMPLE: TRIFLURIDINE+TIPIRACIL (TT) VS. REGORAFENIB (TT BETTER TOLERANCE)

Medication possession ratio:
TT OR 2.47

Proportion of days covered:
TT OR 2.77

TT 83%,
Regorafenib 68%

TT HR 0.76

Data on adherence must be taken into account!

Patel Anuj K, Barghout Victoria, *et al.* Real-Word Adherence in Patients with Metastatic Colorectal Cancer Treated with Trifluridine plus Tipiracil or Regorafenib. *The Oncologist* 2020

Adherence to oral chemotherapy medications among GI cancer patients

117 patients with GI cancer

Only 56% good medication adherence

FACTORS ASSOCIATED TO NON-ADHERENCE

History of patient-caused treatment interruptions due to worsening of symptoms

Diarrhea

Pain

Taking oral chemo every 8h

Diminished sense of priority for medication

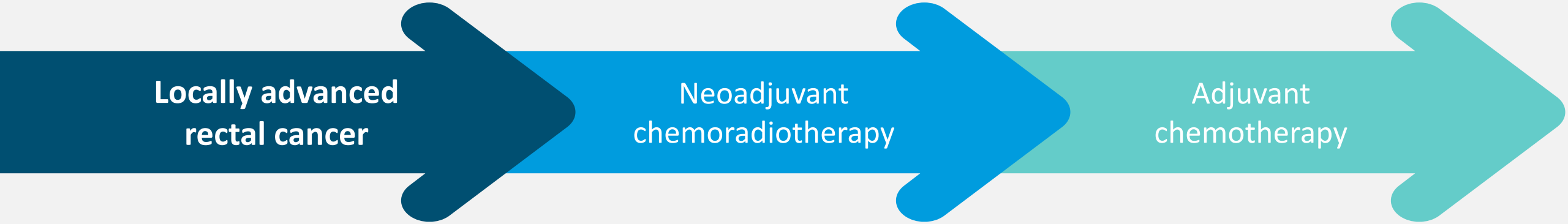
Hirao Chieko, Mikoshiba Naoko, *et al*. Adherence to oral chemotherapy medications among gastroenterological cancer patients visiting an outpatient clinic. *Japanese Journal Clinical Oncology.* 2017;1-9

Outcomes and adherence

Example: Association of treatment adherence with oncologic outcomes for patients with rectal cancer

POST HOC ANALYSIS OF THE CAO/ARO/AIO-04 PHASE 3 RANDOMIZED CLINICAL TRIAL (1232 PATIENTS)

2 groups: With/without oxaliplatin



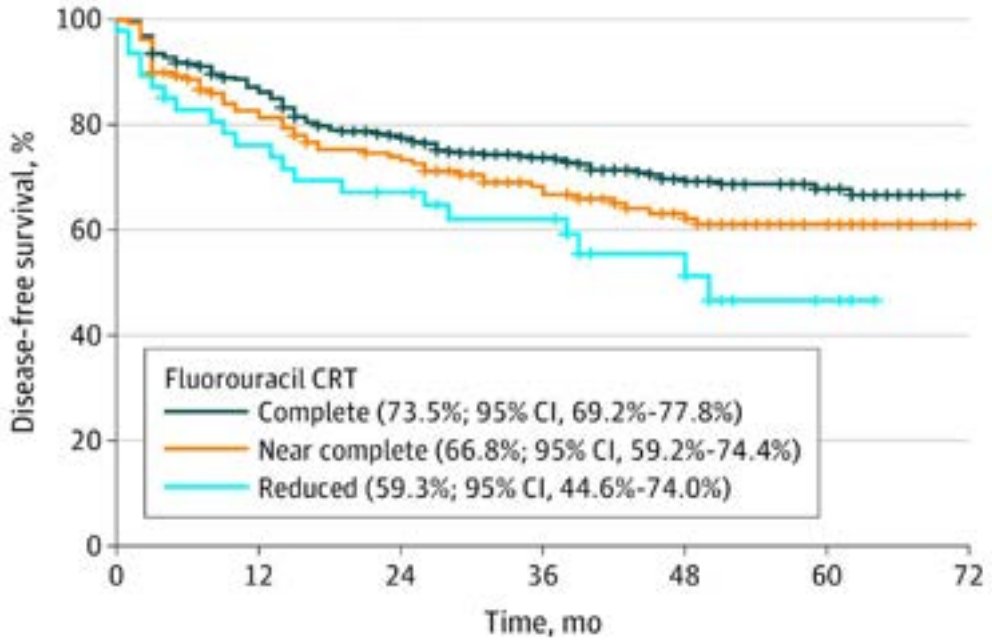
Disease-free survival

Diefenhardt Markus, Ludmir Athan, *et al*. Association of Treatment Adherence With Oncologic Outcomes for Patients with Rectal Cancer. *JAMA oncology* 2020;6:1416-1421

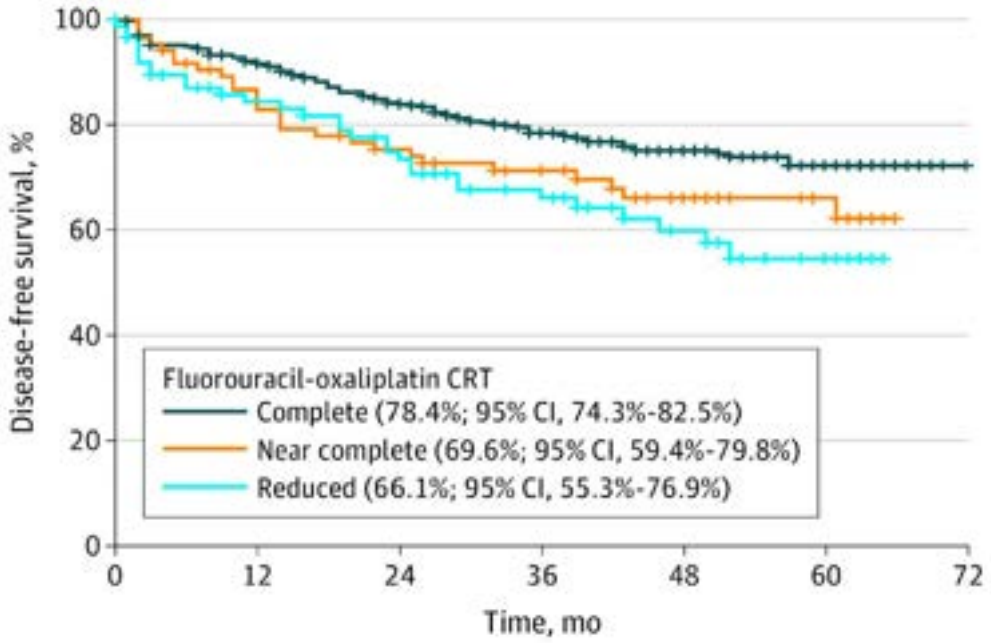
Outcomes and adherence

Neoadjuvant treatment

A NEOADJUVANT FLUOROURACIL CRT



B NEOADJUVANT FLUOROURACIL-OXALIPLATIN CRT



No differences in adjuvant chemo

Diefenhardt Markus, Ludmir Athan, *et al.* Association of Treatment Adherence With Oncologic Outcomes for Patients with Rectal Cancer. *JAMA oncology* 2020;6:1416-1421

Conclusions, the paradox of non-adherence to treatment in oncology

We are experiencing a fascinating time in oncology: Targeted and highly effective treatments, easier to administer and safer

However, this is associated with adherence problems

Studies are heterogeneous, some of them biased, but nonadherence is frequent

The causes of nonadherence are complex, involving patient, disease, and treatment factors

Data on adherence must be considered and addressed with the patient. Strategies to improve adherence must be part of the management of neoplastic diseases