Complications arising with compliance

Dr. Andrea Antonuzzo

Supportive Care Unit
Medical Oncology 1 - Polo Oncologico
Azienda Ospedaliero-Universitaria Pisana
Pisa - Italy
Faculty disclosure

I have no conflict of interest to declare
1. Definitions

Compliance
Adherence
Concordance
Persistence
Definitions: compliance

Respect of physician’s indications

Degree of coincidence between patient’s attitude (in terms of drugs intake, dietary, lifestyle) and physician’s indications

(Paternalistic view)
Definitions: adherence

Active and collaborative patient’s involvement

Planned and informed-based treatment (“concordance and persistence”)

Defined as “the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage and frequency”

Term preferred to compliance because is generally believed to have a less pejorative and less judgmental connotation

Value Health 2008
WHO’s Five Dimensions of Adherence

- Social & Economic
- Patient Related
- Therapy Related
- Condition Related
- Health Care System
Definitions: Concordance and Persistence

Concordance: the need to reach a therapeutic alliance between physician and patient respecting both

Persistence: length of time in which the patient does follow recommendations
Adherence, Compliance, and Persistence

Adherence

Drug Prescription

Discontinuation

End Prescription

Compliance

Persistence (days)

Time
2. Factors influencing treatment’s adherence
Adherence to anticancer agents has become problematic because of:

Increased *combinations of oral (biologic/targeted) therapy* with varying patterns of administration and duration of use

*Poly-pharmacy*

*Older baseline age* of patients with cancer
Other factors influencing treatment’s adherence

Social and economics (e.g. poverty and income)

Health care systems factors (organizational structures and characteristics of healthcare professionals)

Patient (Motivation, attitude, knowledge, beliefs, perceptions and expectations)
The importance of treatment’s adherence

Overestimation by patients and physicians of adherence to treatments, specifically for oral therapies.

Reduced compliance gives increased costs for Healthcare system.

Non adherence to treatments varies due to disease and phase of treatment.

Importance of evaluating strategies for improving compliance.
Signs and predictors of poor adherence and persistence

- Missed appointments, inadequate follow-up
- Poor patient-provider relationship
- Unfilled prescriptions
- Adverse effects from medication, medication cost
- Lack of belief in treatment
- Psychologic problems, particularly depression
Reasons For Not Taking Medications

- Forgot to take
- Symptoms disappeared
- Wanted to save money
- Considered drug ineffective
- Didn’t need them
- Didn’t like side effects
- Drug prevented other activities
- Had no Rx reminder
- Problem getting Rx filled

Wall Street Journal Online, Harris Interactive 2005
The complexity of non-adherence

Non-adherence is complex, with many influences:

- Reasons are systematic, medical, and individual in origin
- Self mgmt behaviors
- Mental state
- Motivation
- Depression
- Low health literacy
- Organizational skills
- Stress
- Worry
- Cost, income
- Relationship with caregivers
- Social support structure
- Asymptomatic disease
- Side effects
- Multiple conditions
- Complex medical regimens

So solutions must be analytical, multifaceted
Models of adherence and persistence

- **Personal Factors**
  - Emotional state
  - Health beliefs
  - Social supports
  - Feelings about disease, self-efficacy & outcome expectations
  - Socioeconomic status

- **Treatment Factors**
  - Reason for therapy
  - Schedule
  - Immediacy & evidence of benefit
  - Side effects
  - Costs

- **Interaction With System**
  - Relationship with providers
  - Satisfaction with care
  - Insurance coverage
  - Convenience of clinics

**ADHERENCE & PERSISTENCE**
3. The history...(of adherence) and literature
Adult populations

Adult pts with non oncological chronic disease on average take only \textit{half of their prescribed medications}

Adherence and persistence have been traditionally \textit{assumed to be better in cancer pts} due to the perceived understanding of the risk of not taking medications as prescribed

Adherence and non–oncological Chronic diseases

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Adherence to Medication

Lars Osterberg, M.D., and Terrence Blaschke, M.D.

Drugs don’t work in patients who don’t take them.

— C. Everett Koop, M.D.

HIV, Hypertension, Psychiatric illnesses, pediatric pts
Adherence and symptoms and comorbidities Tx

- Pain
- Anorexia-asthenia
- Nausea and vomiting
- Constipation-diarrhea
- Gastrointestinal obstruction
- Ascites
- Dyspnea

- CV and tromboembolic diseases, diabetes, psychiatric/neurologic, …
<table>
<thead>
<tr>
<th>YEAR</th>
<th>CANCER</th>
<th>NO.</th>
<th>ORAL THERAPY</th>
<th>ADHERENCE OR PERSISTENCE MEASURE</th>
<th>ADHERENCE OR PERSISTENCE RATE</th>
<th>TIME PERIOD</th>
<th>STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>Hematologic malignancy</td>
<td>108</td>
<td>Prednisone and allopurinol</td>
<td>Serum metabolites</td>
<td>Prednisone: 26.8% Allopurinol: 16.8%</td>
<td>6 mo</td>
<td>Levine 1987(^5^); Richardson 1988</td>
</tr>
<tr>
<td>1990</td>
<td>Breast cancer</td>
<td>51</td>
<td>Cyclophosphamide and/or prednisone</td>
<td>Self-report that 90-110% taken</td>
<td>53% overall with both drugs</td>
<td>6 mo</td>
<td>Lebovits 1990(^2^)</td>
</tr>
<tr>
<td>1992</td>
<td>Lymphoma</td>
<td>21</td>
<td>Chlorambucil, prednisolone, or dexamethasone</td>
<td>Microelectronic monitoring system (MEMS)</td>
<td>100% (standard deviation [SD]; 20.6%)</td>
<td>852 d</td>
<td>Lee 1992(^5^)</td>
</tr>
<tr>
<td>1993</td>
<td>Breast cancer</td>
<td>26</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>97.9% (SD: 3%) by self-report; 92.1% (SD: 9.8%) by pill counts; 85.4% (SD: 17.2%) by MEMS</td>
<td>Mean of 2.92 mo</td>
<td>Waterhouse 1993(^4^)</td>
</tr>
<tr>
<td>1993</td>
<td>Small cell lung cancer</td>
<td>12</td>
<td>Etoposide</td>
<td>MEMS</td>
<td>93.2% (SD: 12%)</td>
<td>298 d</td>
<td>Lee 1993(^6^)</td>
</tr>
<tr>
<td>1996</td>
<td>Ovarian cancer</td>
<td>11</td>
<td>Altretamine</td>
<td>MEMS</td>
<td>97.4% (SD: 6.9%)</td>
<td>294 d</td>
<td>Lee 1996(^4^)</td>
</tr>
<tr>
<td>2000</td>
<td>Colon cancer</td>
<td>57</td>
<td>Uracil-tegafur</td>
<td>Self-report Physician interview Urine level</td>
<td>94.4% at 3 mo, 94.7% at 1 y by self-report and interview; 94.7% in range by urine testing of 38 patients at various timepoints</td>
<td>1 y</td>
<td>Sadahiro 2000(^5^)</td>
</tr>
<tr>
<td>2002</td>
<td>Breast cancer</td>
<td>53</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>76% missed &lt;1 dose per wk</td>
<td>6 mo</td>
<td>Murthy 2002(^6^)</td>
</tr>
<tr>
<td>2003</td>
<td>Breast cancer</td>
<td>2,378</td>
<td>Tamoxifen</td>
<td>Prescription refill records</td>
<td>77% filled prescriptions that covered at least 80% of doses over the 1st y; 50% did so by 4th y</td>
<td>4 y</td>
<td>Partridge 2003(^7^)</td>
</tr>
<tr>
<td>2005</td>
<td>Breast cancer</td>
<td>110</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>88% adherent</td>
<td>Not stated</td>
<td>Grunfeld 2005(^8^)</td>
</tr>
<tr>
<td>2006</td>
<td>Myelodysplastic syndrome</td>
<td>90</td>
<td>Topotecan</td>
<td>MEMS</td>
<td>90%</td>
<td>5-10 d</td>
<td>Klein 2006(^9^)</td>
</tr>
<tr>
<td>2006</td>
<td>Breast cancer</td>
<td>131</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>55% reported nonadherence to medication frequently or occasionally</td>
<td>Single point in time</td>
<td>Atkins 2006(^6^)</td>
</tr>
<tr>
<td>2007</td>
<td>Breast cancer</td>
<td>2,816</td>
<td>Tamoxifen</td>
<td>Prescription refill records</td>
<td>77.9% at 1 y; 64.8% at 3.5 y</td>
<td>3.5 y</td>
<td>Barron 2007(^6^)</td>
</tr>
<tr>
<td>2007</td>
<td>Breast cancer</td>
<td>1,633</td>
<td>Tamoxifen</td>
<td>Clinical notes, audit records, cancer registry data, prescription records</td>
<td>93% median (95% confidence interval, 84-100%)</td>
<td>2.4 y</td>
<td>Thompson 2007(^8^)</td>
</tr>
<tr>
<td>2008</td>
<td>Breast cancer</td>
<td>12,391</td>
<td>Anastrozole</td>
<td>Prescription refill records</td>
<td>78-85% of d were covered by filled prescriptions in Year 1; 62-79% of d were covered by filled prescriptions in Year 3</td>
<td>3 y</td>
<td>Partridge 2008(^6^)</td>
</tr>
<tr>
<td>2008</td>
<td>Breast cancer</td>
<td>161</td>
<td>Capecitabine</td>
<td>MEMS</td>
<td>76% took at least 80% of doses</td>
<td>6 cycles (14/21 d)</td>
<td>Partridge 2008(^7^)</td>
</tr>
</tbody>
</table>

**NOTE:** Adapted and updated from Partridge 2002.\(^9^\)
Adherence and oral anticancer Tx: imatinib

In GIST as in CML **adherence to Imatinib is not optimal**

Response correlated to adherence

General perception of adherence to therapy among patients, physicians and third persons (spouse, family, etc.) was uniformly *higher than reality*
So adherence is important because...

The percentage of prescribed imatinib taken averaged 90.9% with 71.0% of patients taking less (down to 29%) but also 14.8% taking more than prescribed (up to 202%).

Only 14.2% were perfectly adherent with 100% of prescribed imatinib taken...
### Adherence and breast cancer hormonaltx

#### Table 2 Multivariate logistic regression model—factors associated with hormone use at 36 months after breast cancer diagnosis (N = 303)

<table>
<thead>
<tr>
<th>Factor</th>
<th>AOR</th>
<th>P value</th>
<th>Adjusted adherence rate % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04</td>
<td>0.13</td>
<td>86.7 (86.1, 87.3)</td>
</tr>
<tr>
<td>40</td>
<td></td>
<td></td>
<td>90.6 (90.2, 91.1)</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td>93.4 (93.2, 93.8)</td>
</tr>
<tr>
<td>60</td>
<td></td>
<td></td>
<td>97.0 (96.8, 97.1)</td>
</tr>
<tr>
<td>Comorbidity (any)</td>
<td>3.14</td>
<td>0.03</td>
<td>97.0 (91.8, 98.9)</td>
</tr>
<tr>
<td>Partnership (no)</td>
<td>0.84</td>
<td>0.71</td>
<td>89.5 (77.4, 95.5)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>0.98</td>
<td>0.01</td>
<td>98.9 (96.1, 99.7)</td>
</tr>
<tr>
<td>Less-acculturated Latina</td>
<td>9.08</td>
<td>0.001</td>
<td>98.9 (96.1, 99.7)</td>
</tr>
<tr>
<td>More-acculturated Latina</td>
<td>3.42</td>
<td>0.28</td>
<td>97.2 (78.6, 99.7)</td>
</tr>
<tr>
<td>Other</td>
<td>3.74</td>
<td>0.06</td>
<td>97.4 (90.6, 99.3)</td>
</tr>
<tr>
<td>High school graduated (yes)</td>
<td>0.94</td>
<td>0.91</td>
<td>91.5 (77.9, 97.1)</td>
</tr>
<tr>
<td>Health insurance (no)</td>
<td>0.12</td>
<td>0.001</td>
<td>55.8 (26.0, 82.0)</td>
</tr>
<tr>
<td>Stage(I)</td>
<td>1.00</td>
<td>0.99</td>
<td>91.1 (78.0, 96.7)</td>
</tr>
<tr>
<td>Radiation therapy (yes)</td>
<td>0.47</td>
<td>0.18</td>
<td>82.7 (61.8, 93.4)</td>
</tr>
</tbody>
</table>

#### Health insurance (no) | 0.12 | 0.001 | 55.8 (26.0, 82.0) |
Stage(I) | 1.00 | 0.99 | 91.1 (78.0, 96.7) |
Radiation therapy (yes) | 0.47 | 0.18 | 82.7 (61.8, 93.4) |
Chemotherapy (yes) | 1.59 | 0.44 | 91.0 (76.0, 97.0) |
Mastectomy (yes) | 0.79 | 0.61 | 88.9 (76.8, 97.0) |
Hormone side-effects (yes) | 0.26 | 0.003 | 72.7 (52.4, 86.6) |
Financial adequacy (yes) | 0.97 | 0.95 | 90.8 (80.3, 96.0) |
Discussion of hormone therapy (yes) | 0.95 | 0.92 | 96.7 (90.8, 98.8) |
PEPPi\(^b\) (range 0–50) | 1.04 | 0.04 | 71.6 (70.9, 72.3) |
Patient-centered communication (range 4–16) | 1.22 | 0.006 | 59.1 (55.6, 62.5) |

\(^b\) Predominantly Asian Pacific American and Spanish-speaking Mexican American women.
The importance of treatment’s adherence: Elderly patients

Factors influencing adherence to cancer treatment in older adults with cancer: a systematic review

M. T. E. Puts¹*, H. A. Tu¹,², A. Tourangeau¹, D. Howell¹,³, M. Fitch¹,⁴, E. Springall⁵ & S. M. H. Alibhai⁶,⁷
The importance of treatment’s adherence: elderly patients

Older adults have numerous comorbidities as well as cognitive and sensory impairment that may affect adherence

...focused mainly on women with breast cancer and adherence to adj hormonal tx

Adherence rate varied from 52% to 100% and only one study asked reasons for non adherence

Non-adherence was common across studies but little is known about the factors influencing non-adherence. More research is needed....
Adherence and persistence rates ranged from 16% to 100% with different therapies and different methods of measurement.

Ca Cancer J Clin 2009
The importance of treatment’s adherence

Cancer Treatment Reviews

Anti-Tumour Treatment

Adherence enhancing interventions for oral anticancer agents: A systematic review

Tim Mathes *, Sunya-Lee Antoine¹, Dawid Pieper², Michaela Eikermann³

Institute for Research in Operative Medicine, Faculty of Health – School of Medicine, Witten/Herdecke University, Ostmerheimer Str. 200, Building 33, D-51
Systematic review of treatment’s adherence: examined studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Adherence measurement</th>
<th>Adherence definition</th>
<th>Mean adherence rate (IG/CG (p))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khandelwal 2012</td>
<td>Prescription refill</td>
<td>Doses taken</td>
<td>44.8/41.5 (0.402)</td>
</tr>
<tr>
<td>Levine 1987</td>
<td>Drug levels in serum (prednisone)</td>
<td>Drug levels in serum within individuals profile range</td>
<td>38.0/32.7/37.8/26.8 (p &lt; 0.01 for each comparison)</td>
</tr>
<tr>
<td>Richardson 1987</td>
<td>Drug levels in serum (prednisolone)</td>
<td>Drug levels in serum within individuals profile range</td>
<td>41.7/41.1/59.5/21.9 (p &lt; 0.01 for each IG vs. CG; p &lt; 0.01 for IG1 and IG2 versus IG3)</td>
</tr>
<tr>
<td>Macintosh 2007</td>
<td>Pill count</td>
<td>Drug levels in serum within individuals profile range</td>
<td>33.8/36.1/35.8/31.2 (p &lt; 0.05 for each comparison)</td>
</tr>
<tr>
<td>Moon 2012</td>
<td>NR</td>
<td>Drug levels in serum within individuals profile range</td>
<td>38.8/49.0/56.6/24.8 (p &lt; 0.05 for each comparison)</td>
</tr>
<tr>
<td>Simons 2011</td>
<td>Medication event monitoring system</td>
<td>Doses taken</td>
<td>81/86 (NS)</td>
</tr>
<tr>
<td>Tschida 2012</td>
<td>Prescription refill</td>
<td>Doses taken</td>
<td>96.5/96.6 (0.958)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days with correct intake (not specified)</td>
<td>97.9/90.5 (0.069)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients with ≥80% intake</td>
<td>96.8/87.2 (0.029)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients with ≥90% intake</td>
<td>100/79 (NR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days with ≥80% intake</td>
<td>92/75 (NR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Days with ≥90% intake</td>
<td>100/75 (NR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Irregular intake intervals (&gt;14h or &lt;10h)</td>
<td>RR = 0.51 (&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doses taken</td>
<td>65.7/58.0 (&lt;0.001)</td>
</tr>
</tbody>
</table>

NR: not reported; NS: not significant; RR: relative risk

Cancer Treat Rev 2013
Systematic review of treatment’s adherence: conclusions

Adherence enhancing interventions could have a promising effect *(educational and counseling → mostly target several of the adherence dimension…)*

Crucial point: baseline adherence when choosing patients to avoid ceiling effects

Limited evidence: lack of sufficient studies and partly inconsistent results

*Cancer Treat Rev 2013*
4. Complications arising with compliance (adherence)
Complications arising with adherence

About one quarter of newly developed anticancer agents could be taken orally.

Adherence is lower in patients taking oral anticancer agents compared to patients taking intravenous chemotherapy.
New toxicities…

CA Cancer J Clin, 2013

26-30 September 2014, Madrid, Spain
How to monitor adherence (toxicity, dose reductions, drug interactions)

<table>
<thead>
<tr>
<th>TABLE 3. Methods Available To Monitor Adherence (^1,^2,^15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Methods</td>
</tr>
<tr>
<td>Direct observation of therapy</td>
</tr>
<tr>
<td>Measurement of medicine levels (or a metabolite) in the blood</td>
</tr>
<tr>
<td>Measurement of a biologic marker in the blood</td>
</tr>
<tr>
<td>Measurement of physiologic markers</td>
</tr>
<tr>
<td>Assessment of clinical response</td>
</tr>
<tr>
<td>Indirect Methods</td>
</tr>
<tr>
<td>Questionnaires/self-reports</td>
</tr>
<tr>
<td>Diaries</td>
</tr>
<tr>
<td>Pill counts</td>
</tr>
<tr>
<td>Prescription refill records</td>
</tr>
</tbody>
</table>
Drugs and adherence

There are little data in oncology published to date regarding the effects of non-adherence and non-persistence. The importance of non-adherence likely varies from drug to drug.

Evidence for Therapeutic Drug Monitoring of Targeted Anticancer Therapies
Bo Gao, Shang Yeap, Arthur Clements, Bavanthi Balakrishna, Mark Wong, and Howard Gurney
Diagnosing Toxicity

In many cases, drug toxicity can be diagnosed clinically.
Diagnosing Toxicity

On the other hand, some adverse effects such as lethargy, anorexia, and diarrhea are non-specific, and the causality of which can be difficult to differentiate from malignancy or complicating treatments, including antibiotics and analgesics.

Drug concentration monitoring may be useful in delineating whether these symptoms are related to the targeted agent or to other causes.
Monitoring Dose Reductions

Although dose reductions of TKIs as a result of toxicity are common, determination of the appropriate extent of dose reductions to prevent an ineffective dosage is often difficult.

Importance to prevent an “overshoot” and also provide important reassurance to patients and oncologists about appropriate dosing.
Detecting Drug Interactions

**Polypharmacy** is common in patients with cancer who often commence new drugs during anticancer treatment.

**Potential drug interactions** (especially with CYP3A4 and ABCB1 inhibitors and inducers, have been shown to affect TKI exposure)

It becomes increasingly important to identify patients who require dose modifications to achieve adequate therapeutic drug exposure while minimizing risk of toxicity.
Effects of non-adherence

Non adherence can contribute greatly to:

*Variability* observed in drug’s therapeutic effect

*Erroneous conclusions* with unnecessary diagnostic testing, hospitalizations and cessation of an active treatment

*Over-adherence* to self-administered medications

*Patient’s “more is better” approach or confusion* led to overdosing and to substantially increased toxicity
“Economic effects” of non-adherence

Curing nonadherence would cover the cost of healthcare for 44.8 million Americans.

50% 700 THOUSAND $290 BILLION

On average 50 percent of patients do not take their medications as prescribed and 33 percent never even fill their first prescription.

Each year, an estimated 700,000 Americans experience adverse reactions to prescribed drugs that require an emergency room visit.

The estimated annual cost of patients not taking their medications as prescribed approaches $290 billion.

Annual U.S. cost estimates for non-adherence range from $100-$300 billion.
Effects of non-adherence: clinical case -1

56 yrs old pts with metastatic breast cancer (bone, liver SNC)
Second line CT with oral Navelbine and Capecitabine + Denosumab
4 consecutive days of oral NVB (instead of 1!!!)
For this patient probably the i.v. drugs should be better.... (“cognitive impairment due to brain mts treated with RT”)
Effects of non-adherence: clinical case -2

66 yrs old pts with metastatic renal cancer
Second line therapy with Sorafenib at a reduced dose (50%)
Grade 1-2 diarrhoea with loperamide therapy and continuation of treatment → 4 kg weight loss, severe astenia and anorexia → stop Tx
Effects of non-adherence: clinical case -3

Case Study

A 50-year-old woman with metastatic breast cancer is prescribed capecitabine 1250 mg/m² by her medical oncologist. The physician instructs her to take four 500 mg tablets in the morning and four 500 mg tablets in the evening for 14 days, take 7 days off, return to the clinic in 3 weeks for a follow-up appointment, and to call if she has any problems.

Three weeks later the patient returns to the clinic with painful erythema and swelling of the hands along with diarrhea which caused her to miss several days of work. She also complained of nausea. She said she began taking antacids with her medication to help the nausea but it did not improve. She stated that she stopped taking her capecitabine with four days left to go because she felt so miserable. When asked why she did not call the clinic, the patient stated “I did not want to bother anyone and I thought everyone gets sick with chemotherapy.”

Oncology Issues, 2008
5. Strategies to improve compliance (adherence)
Strategies to improve adherence
Protection of Patients, Family, and Caregivers

Patients should be educated about any requirements for storage, such as temperature or light-resistant needs. The patient, family, and caregiver also should be instructed on safe practices with administration of oral chemotherapy, adjustments in dosing, or return of drug to the pharmacy or oncology clinic. Patient education sheets should be available to enhance verbal instructions with reinforcement that oral anticancer agents are toxic substances.

Moody & Jackowski, 2010
Prescribing Precautions

The importance of detailed education by the oncology team, including simple calendars and detailed written instructions for disposal of hazardous medication.
Accuracy

For each drug, **major steps** are focused on the **prescribing, dispensing, administering, and monitoring** stages of medication use.

*Weingart et al., 2011*
Side-effect reporting

A mechanism of side-effect reporting is essential to capture patient-reported outcome data and may include a simple diary.

Patients may minimize experienced symptoms over a two- to three-week period;

If the clinic visit interval is greater than three weeks, patients may possibly forget symptoms.
Strategies to improve adherence

Made by patient:
Patient’s support programs
Computerized “Drug alerts”

Made by physician:
Improving of patient-physician’s communication
Regimen’s simplification
Increase of follow up visits
Frequent phone contacts
Other strategies to improve adherence
Figure 1

Three Pillars of Improved Adherence

1. Improve Drug Regimen
   - Follow up
   - Make/Recommend changes; share information with MD
   - Conduct comprehensive medication review
   - Understand patient experiences and preferences
   - Create accurate medication use profile

2. Reduce Cost Barriers
   - VBP
   - Formulary compliance
   - Generics
   - Prescription Assistance Programs

3. Address Patient Behavior
   - Follow up
   - Engage patients in the care process
   - Address patient preferences, limitations and priorities
   - Educate patients about their condition, how and why to take medications

Appropriate Medication Use

Strategies to improve adherence: the role of Supportive Care Units

Implementing Supportive Medical therapy for patient, from diagnosis and all across the route of care (adjuvant/palliative), for the cure of adverse events, toxicities and co-morbidities, to maintain psyco-physical well-being and improving adherence to care protocols or treatment in terms of dose intensity and interval of administration.
6. Open questions and discussion
Discussion

Many new drugs (targeted and non) with a lot of new and (probably) under-described toxicities

Small data about long-term safety of new drugs

Two suggested lines for improvement:

1. **Scientific** (ad hoc designed studies for adherence evaluation)
2. **Managerial** (empowerment of supportive care programs and services)
Open questions: scientific

Tools to better evaluate adherence

Who does judge toxicities? Patient or physician?
With new targeted: are we using the correct toxicity scale?

Fast track drug approval conditioning adequate toxicity reports (specific populations—third toxicity axis—late adverse events)

Studies regarding the impact of the better supportive care and its impact in adherence and outcome improvements
Open questions: scientific

*Internal guidelines* for each center to define patient’s adherence

*Prospective studies* as tools of patient’s toxicity/adherence evaluation, mHealth

Need of *prospective, observational/interventional studies* about adequate supportive care
Discussion

Difficult to Swallow: Issues Affecting Optimal Adherence to Oral Anticancer Agents

Winson Y. Cheung, MD, MPH

OVERVIEW

The number of anticancer drugs currently available in oral formulation has increased dramatically over the past 15 to 20 years, especially with the recent development of new hormonal and targeted therapies. At present, approximately 25% of all cancer drugs are available in oral formulation, with numbers expected to increase exponentially in the coming years. The convenience associated with the self-administration of oral therapy, the requirement of fewer trips to the physician’s office, and the lack of infusion reactions are all benefits for patients, allowing them to potentially maintain their relative independence while undergoing active anticancer treatment. On the other hand, there are growing concerns regarding patients’ poor adherence to oral therapy as well as the challenges of monitoring patient compliance when treatment administration does not occur in the presence of health care professional (HCPs). More importantly, poor adherence to proven therapies may detrimentally affect the patients’ clinical outcomes, such as survival. Thus, there is an urgent need to identify more effective strategies to measure and monitor adherence to oral anticancer agents in an effort to maximize their therapeutic benefits.
Open questions: managerial

Need of organizative models to better follow patients during anticancer Tx (Supportive Care Units)

Effectiveness of these models not only in Cancer referral centers but also in Secondary and Tertiary Hospitals
Open questions: managerial

Opportunity to improve adherence to Tx and reduce costs for toxicities and drug-non assumption, giving the chance to create a “Sustainable Model of Care” (cost savings for complications and investment for new high cost drugs)

Scientific’s Society warranty (ESMO, MASCC, ASCO,…)

Dedicated working groups
Discussion

Increasing the effectiveness of **ADHERENCE INTERVENTIONS** may have a far **greater impact on the health of the population** than any improvement in specific **medical treatments**.
Thank you for your attention

andrea.antonuzzo@tin.it