

СПбГУ  
Медицинский факультет  
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# Доказательная медицина pros et cons

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# Обучение в ординатуре, начало практики

Ординатор: Почему мы назначаем/делаем именно это?

Куратор:

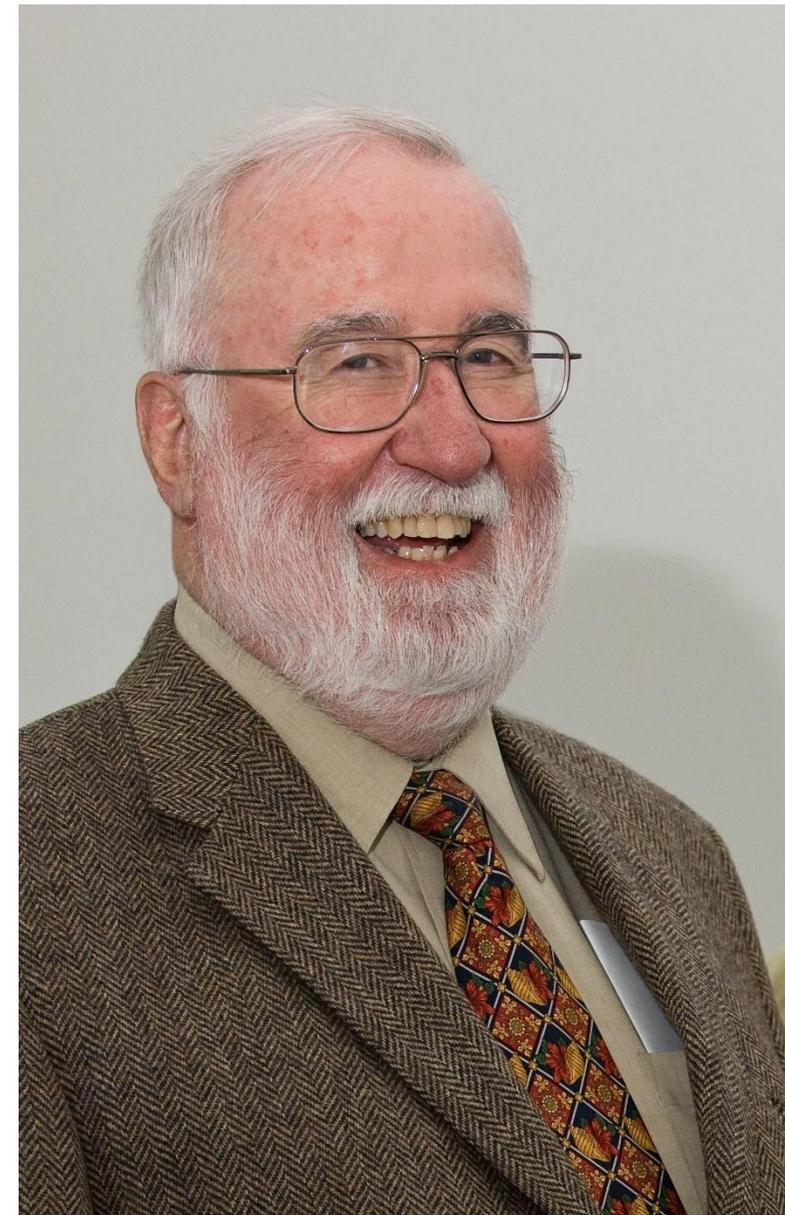
1. В нашем отделении делается так много лет и это работает
2. Так меня научили еще в ординатуре/Университете
3. Это чутье, оно приходит с опытом
4. Профессор X на своей лекции на конф. Y сказал, что он делает так
5. Так написано в RUSSCO (Alarm!Переводчиковой)
6. Так написано в репринте статьи в журнале Z
7. Просто делай так! Слишком много вопросов!

# Доказательная медицина

Evidence based medicine

«The integration of best research evidence with clinical experience and patient values»

*Внедрение в практику данных, полученных из надежных источников с учетом персонального опыта и предпочтений больного.*



David Sackett, 1934-2015

# EBM

- Надежные данные: серьезные клинические исследования
- Личный опыт: персональный и коллективный
- Предпочтения пациента\*: ask tell ask
  - \*NB! Пациента, а не родственников пациента!

# Виды исследований

## 1. Наблюдательные исследования:

- количественные:
  - когортные,
  - случай/контроль,
- качественные:
  - клинический случай,
  - серия клинических случаев

## 2. Клинические исследования:

- рандомизированные контролируемые исследования

## 3. Обзорные исследования:

- количественные: систематический обзор
- качественные: мета-анализ

# Уровни доказательности



*Рис.1. Клиническая фармакология и фармакотерапия в реальной врачебной практике : мастер-класс : учебник / В. И. Петров. - 2011. - 880 с. : ил.*

# Плюсы ДМ

- Наличие статистически достоверных данных
- Большие выборки
- Методология проведения КИ (GCP)
- Четко прописанные протоколы исследований
- Валидированные лаборатории
- Контроль полученных результатов центральными лабораториями
  
- Доступные алгоритмы действий

# Подводные камни ДМ

1. Доказательная медицина высшего уровня доказательности = исследования, спонсированные фармой
2. Допустимо сравнение не с золотым стандартом, а со слабым противником/историческим контролем

# Подводные камни ДМ

3. Нет прямого сравнения похожих препаратов и схем  
(что лучше?)

Пембро или ниво? Карбо+пакли или  
Пеметрексед+Цисплатин?

Одинаковые или разные?

No answer)

# Подводные камни ДМ

4. Статистическая значимость полезных эффектов мб  
минимально полезна в реальности

( + неделя жизни (p 0.001!) vs \$\$\$/Нежелательные явления gr  
3-4)

# Подводные камни ДМ

5. Необязательная публикация отрицательных результатов!

# Подводные камни ДМ

6. Несоответствие пациента КИ реальному пациенту

(ECOG 0-1 с минимальной сопутствующей патологией vs ECOG 2-3 с колоссальной коморбидностью)

7. Невозможность экстраполяции данных КИ в реальную жизнь

# Подводные камни ДМ РФ

8. Ограничение рекомендациями МЗ, ОМС, КСГ и пр.

9. Отсутствие навыка чтения результатов клинических исследований у врачей

- $p < 0.05$
- HR
- Кривые выживаемости
- Водопады
- ???

# Выводы

- Минусы ДМ – не доказательство бессмысленности ДМ
- Принципы ДМ ясны, воспроизводимы и не находятся в кризисе
- Проведение даже маленьких работ по принципам ДМ – хорошо
  
- Нельзя принимать на веру слова учителя
- Нет один раз и навсегда полученного знания - то что верно сегодня, завтра может измениться
- Необходимость постоянного самообразования
- При посещении конференций – важен докладчик, а не тема

# Когда я практикую доказательную медицину?

## 1. Общась с пациентом: SPIKES, PEWTER, ask tell ask

**SPIKES** protocol for delivering bad news:

- ▶ **S** Setting up the interview
- ▶ **P** Assessing the patient's **P**erception
- ▶ **I** Obtaining the patient's **I**nvitation
- ▶ **K** Giving **K**nowledge & info to the patient
- ▶ **E** Addressing patient's **E**motions with empathy
- ▶ **S** Strategy and **S**ummary

Baile et al., 2000



A simple communication technique to help patients feel heard.

- ASK**
  - Always ask permission to begin the conversation.
  - Ask the patient to describe their understanding of the visit with their provider and/or their health. This will help gauge emotions and understanding.
  - Asking helps you determine what the patient hopes to address during the conversation.
- TELL**
  - Provide the information the patient wants to know in manageable bits. Try to use a few short sentences.
  - Share information that is authorized and available.
  - Use simple and clear language, not medical terminology or jargon.
- ASK**
  - Confirm understanding by asking the patient to repeat back information in their own words.
  - Ask if the patient has any questions or wants to know anything else.



# Когда я практикую доказательную медицину?

## 2. Планируя курс лечения пациента \*

- Все ли обследования есть?
- Нужна ли ИГХ?
- Нужна ли МГИ?
- С чего начать:
  - Операция?
  - Лекарственная терапия?
  - BSC?

*\*Споря с коллегами и начальством*

# План лечения

Частая патология -> Уровень доказательности I-II (DISCUSSION)



National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)

## Non-Small Cell Lung Cancer

Version 3.2019 — January 18, 2019

NCCN.org

NCCN Guidelines for Patients® available at [www.nccn.org/patients](http://www.nccn.org/patients)

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### NCCN Guidelines Version 3.2019 Non-Small Cell Lung Cancer

[NCCN Guidelines Index](#)  
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CLINICAL ASSESSMENT

PRETREATMENT EVALUATION

CLINICAL EVALUATION

Stage IIB (T3 invasion, N0)  
Stage IIIA (T4 extension, N0-1; T3, N1; T4, N0-1)

- PFTs (if not previously done)
- Bronchoscopy
- Pathologic mediastinal lymph node evaluation<sup>h</sup>
- Brain MRI with contrast<sup>k</sup>
- MRI with contrast of spine + thoracic inlet for superior sulcus lesions abutting the spine or subclavian vessels
- FDG PET/CT scan<sup>l</sup> (if not previously done)

- Superior sulcus t
- Chest wall
- Proximal airway or mediastinum
- Stage IIIA (T4, N0)
- Unresectable dis
- Metastatic diseases



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### NCCN Guidelines Version 3.2019 Non-Small Cell Lung Cancer

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SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE<sup>a,b</sup>

#### Initial Systemic Therapy Options

Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-1)

- No contraindications to the addition of pembrolizumab or atezolizumab<sup>c</sup>
- Pembrolizumab/carboplatin/pemetrexed (category 1)<sup>1,2,d</sup> (preferred)
- Pembrolizumab/cisplatin/pemetrexed (category 1)<sup>2,d</sup> (preferred)
- Atezolizumab/carboplatin/paclitaxel/bevacizumab (category 1)<sup>3,4,e,f,g</sup>

Contraindications to the addition of pembrolizumab or atezolizumab<sup>c</sup>

- Bevacizumab/carboplatin/paclitaxel (category 1)<sup>4,e,f,g</sup>
- Bevacizumab/cisplatin/pemetrexed<sup>4,e,f,g</sup>
- Carboplatin/albumin-bound paclitaxel (category 1)<sup>7</sup>
- Carboplatin/docetaxel (category 1)<sup>8,9</sup>
- Carboplatin/etoposide (category 1)<sup>8,10</sup>
- Carboplatin/gemcitabine (category 1)<sup>11</sup>
- Carboplatin/paclitaxel (category 1)<sup>12</sup>
- Carboplatin/pemetrexed (category 1)<sup>13</sup>
- Cisplatin/docetaxel (category 1)<sup>8</sup>
- Cisplatin/etoposide (category 1)<sup>14</sup>
- Cisplatin/gemcitabine (category 1)<sup>12,15</sup>
- Cisplatin/paclitaxel (category 1)<sup>16</sup>
- Cisplatin/pemetrexed (category 1)<sup>15</sup>
- Gemcitabine/docetaxel (category 1)<sup>17</sup>
- Gemcitabine/vinorelbine (category 1)<sup>18</sup>

Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)

- Albumin-bound paclitaxel<sup>19</sup>
- Carboplatin/albumin-bound paclitaxel<sup>20,21</sup>
- Carboplatin/docetaxel<sup>8</sup>
- Carboplatin/etoposide<sup>8,10</sup>
- Carboplatin/gemcitabine<sup>11</sup>
- Carboplatin/paclitaxel<sup>12</sup>
- Carboplatin/pemetrexed<sup>13</sup>
- Docetaxel<sup>22,23</sup>
- Gemcitabine<sup>24,25</sup>
- Gemcitabine/docetaxel<sup>17</sup>
- Gemcitabine/vinorelbine<sup>18</sup>
- Paclitaxel<sup>27,28</sup>
- Pemetrexed<sup>30</sup>

<sup>k</sup>If MRI is not possible, CT of head with contrast.

<sup>h</sup>Methods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy.

<sup>l</sup>PET/CT performed skull base to knees or whole body. Positive PET/CT scan findings for distant disease need path scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is

<sup>a</sup>Albumin-bound paclitaxel may be substituted for either paclitaxel or docetaxel in patients who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or for patients where the standard premedications (ie, dexamethasone, H2 blockers, H1 blockers) are contraindicated.

<sup>b</sup>Carboplatin-based regimens are often used for patients with comorbidities or those who cannot tolerate cisplatin.

<sup>c</sup>Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents or presence of an oncogene, which would predict lack of benefit.

<sup>d</sup>If progression on PD-1/PD-L1 inhibitor, switching to another PD-1/PD-L1 inhibitor is not routinely recommended.

<sup>e</sup>Bevacizumab should be given until progression.

<sup>f</sup>Any regimen with a high risk of thrombocytopenia and the potential risk of bleeding should be used with caution in combination with bevacizumab.

<sup>g</sup>Criteria for treatment with bevacizumab: non-squamous NSCLC, and no recent history of hemoptysis. Bevacizumab should not be given as a single agent, unless as maintenance if initially used with chemotherapy.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

# План лечения

- Редкая патология
- сойдет уровень и поменьше, Case report

НЕ ТОЛЬКО МНЕНИЕ  
ПРОФЕССОРА-ЭКСПЕРТОВ

## CASE REPORT

Open Access

### Inflammatory myofibroblastic tumor of the lung- a case report

Chien-Kuang Chen<sup>1</sup>, Chia-Ing Jan<sup>2</sup>, Jian-Shun Tsai<sup>1</sup>, Hsu-Chih Huang<sup>1</sup>, Pin-Ru Chen<sup>1</sup>, Yu-Sen Lin<sup>1</sup>, Chih-Yi Chen<sup>1</sup>, Hsin-Yuan Fang<sup>1\*</sup>

#### Abstract

A 45-year-old man presented with a six-month history of progressive dyspnea with productive cough and wheezing. The patient was a heavy smoker and had a history of tongue cancer, hypertension, and asthma. Chest X-ray and computed tomography showed a mass lesion in the left hilar region and total collapse of the upper left lobe of the lung. Bronchoscopy revealed a whitish solid tumor obstructing the left upper lobe bronchus. Positron emission tomography showed increased tracer uptake in the lesion. A thoracoscopic lobectomy of the left upper lobe of the lung was performed. The final pathologic diagnosis was inflammatory myofibroblastic tumor.

#### Introduction

Inflammatory myofibroblastic tumor (IMT) of the lung, also known as plasma cell granuloma or inflammatory pseudotumor, is a rare disease entity [1]. Diagnosis of IMT is difficult to establish before surgery because of its diversified radiologic manifestations. This tumor can be cystic or homogeneous, endobronchial or parenchymal with or without clear margins [2]. Complete surgical resection is the treatment of choice not only to exclude malignancy but also to achieve a good prognosis [3,4]. We report a case of inflammatory myofibroblastic tumor that was successfully removed by thoracoscopic lobectomy.

#### Case report

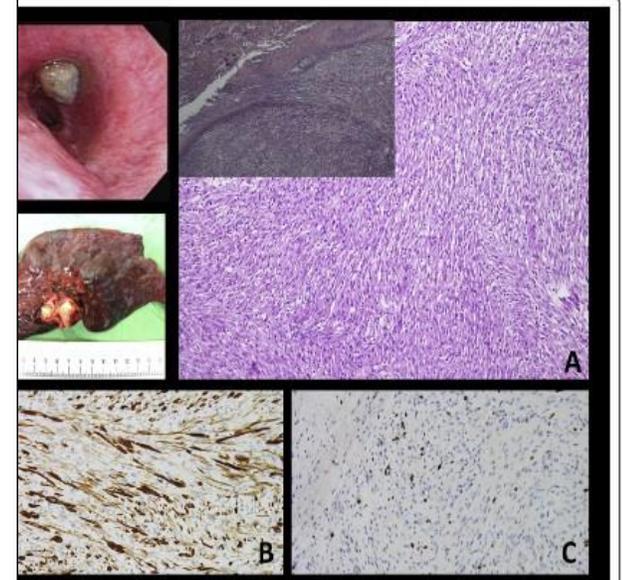
A 45-year-old man presented with a 6-month history of progressive dyspnea with productive cough and wheezing. The patient had a history of smoking (1 pack per day for 20 years), hypertension and asthma, which was under regular medical control. He also had a history of tongue cancer (squamous cell carcinoma, pT2N0M0, stage II) for which he underwent wide excision of the right side of the tongue and modified neck lymph node dissection five years prior to this presentation. Chest plain film showed a protruding mass shadow in the left hilar region. Costodiaphragmatic angles

were clear. There was increased density over left lung field with elevation of the left side of the diaphragm. These features were indicative of a hilar mass obstructing the bronchus with collapse of the upper left lobe of the lung (Fig. 1A). Contrast enhanced computed tomography (CT) showed a hilar mass measuring approximately 35 mm × 28 mm × 15 mm and a collapsed left upper lobe of the lung. There was weak enhancement in the arterial phase. The endobronchial part of the tumor had clear margins along the bronchus of the upper left lobe of the lung. The distal part of the tumor had indistinct margins along the lung parenchyma. The distal bronchus was dilated and filled with secretions. There was no mediastinal lymphadenopathy (Fig. 1B). Bronchoscopy revealed a whitish tumor obstructing the left upper bronchus (Fig. 2). Biopsy specimens of the tumor taken during the bronchoscopy examination showed evidence of smooth muscle cell proliferation with focal abnormal mitosis. A smooth muscle cell tumor of malignant potential was considered. Positron emission tomography (PET) showed increased fluoro-deoxyglucose (FDG) uptake in the lesion (Fig. 1C).

The tumor involved the upper left lobe of the lung and obstructed the bronchus. The patient underwent a thoracoscopic lobectomy under general anesthesia with double lumen endotracheal tube placement. The vessels of the left upper lobe were divided and ligated using an endoscopic autostapling device. The bronchus of the upper left lobe was opened by endoscissor. The cutting margin was checked by examination of frozen sections

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Thoracoscopic exam shows a whitish tumor obstructing the left upper bronchus. Gross. The tumor impacted the whole left upper lobe of the lung. Microscopically, the biopsy specimen is composed of spindle cells with fibroblastic and myofibroblastic features arranged in fascicles. (A) The tumor is mostly limited within the bronchi. In a few foci, pushing of tumor margin to the lung is noted (×20; ×100). Immunohistochemical study demonstrated (B) vimentin (v) (×200), and (C) cytokeratin (ck) (×200).

Diagnosis of IMT is difficult to establish before surgery because of its diversified radiologic manifestations; it can be difficult to distinguish from malignancies on small tissue samples obtained from bronchoscopic examination or needle biopsy. In fact, IMT cases are diagnosed based on analysis of specimens alone [6]. In addition, IMT is often differentiated from other neoplasms on PET because of the high uptake of tracer in IMT. The diagnosis of IMT is dependent on tumor size (less than 3 cm) and complete surgical resection. The overall survival rate is about 82% and the overall relapse rate is about 74% [3]. In our case, the

tumor was an endobronchial lesion with clear margins. We were unable to prove whether the tumor involved the lung parenchyma.

Surgical management of lesions in the major bronchi is challenging. In our patient, we performed a thoracoscopic technique to cut the adhesion of the major fissure, superior pulmonary vein and pulmonary artery branches to upper lobe of the lung. We then opened the left upper bronchus to confirm that the cut end of the bronchus was free. The bronchus was closed with interrupted sutures.

IMT is characterized histologically by spindle cell proliferation. The tumor is referred to by different names

# Когда я практикую доказательную медицину?

## 3. Оценивая эффект лечения

КТ/МРТ/ ПЭТ-КТ vs УЗИ, Р

RECIST 1.1, irRECIST



### Key Differences Between RECIST 1.1 and RECIST 1.0

RECIST 1.1 (2009 criteria)	RECIST 1.0 (2000 criteria)
1. Assessment of lymph nodes	1. No specific recommendations
2. Patients with nonmeasurable disease only eligible for studies when the primary endpoint is tumor progression	2. Measurable disease at baseline required
3. Finding of a new lesion should be unequivocal	3. Not specifically defined
4. Imaging of nontarget lesions not necessary at every protocol-specified time point for declaration of partial response or stable disease	4. Not specifically addressed
5. Patient response to treatment need not be confirmed in randomized trials when the primary endpoint is disease progression	5. Patient's initial response to treatment must be confirmed no sooner than four weeks later
6. FDG-PET is "sometimes reasonable to incorporate" as a complement to CT scanning in assessing disease progression	6. No specific recommendations
7. Maximum of five target lesions total and two per organ	7. Maximum of ten target lesions total and five per organ
8. Lesions too small to measure assigned default value of 5mm	8. No specific recommendations
9. Progressive disease requires > 20% increase in sum of diameters from nadir and an absolute increase of > 5mm	9. Progressive disease requires > 20% increase in sum of the longest diameters from nadir—no absolute increase required

Source: Perceptive Informatics.

Table 1. A comparison of RECIST 1.1 and RECIST 1.0.

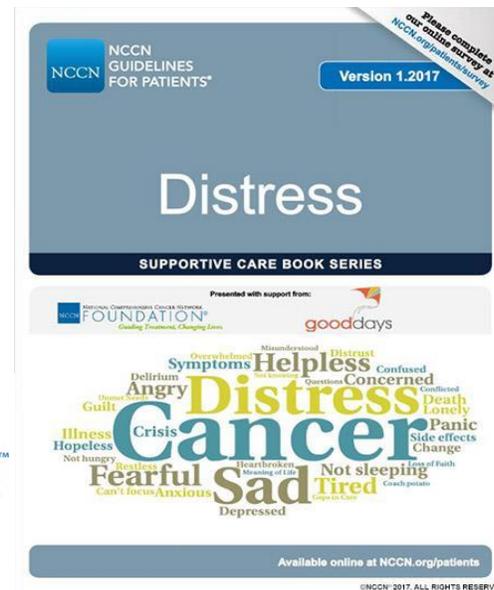
# Когда я практикую доказательную медицину?

## 4. Сталкиваясь с нежелательными явлениями

- Оцениваю значимость побочных эффектов и их связь с препаратом

СТСАЕ

Профилактирую и лечу



# Когда я практикую доказательную медицину?

5. Занимаясь научной деятельностью

Статьи, Литобзоры

В идеальном мире - исследования, диссертации